ANNUAL RESEARCH PROGRESS REPORT, FISCAL YEAR 1975

Rudi Ansbacher, et al

Brooke Army Medical Center
Fort Sam Houston, Texas

1 July 1975

CLINICAL INVESTIGATION SERVICE

Annual Research Progress Report

FISCAL YEAR 1975

Brooke Army Medical Center
Fort Sam Houston, Texas 78234

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FOREWORD

During fiscal year 1975, the Clinical Investigation Service Laboratory, one-half of Ward 43A, Beach Pavilion, was actively utilized to support many of the protocols listed on subsequent pages. Work was begun on the remaining portion of Ward 43A in late FY 75 to add additional laboratory bench space and three administrative offices. This area should be completed by mid FY 76 and will complete the centralization of Clinical Investigation Service activities including administrative functions.

Funds for MEDCASE, capital equipment and consumable supplies continued to be adequate to support the various protocols listed on the following pages.

Thirty-five protocols were registered in fiscal year 1975: 4 were completed, 2 were terminated, and 29 will be ongoing into FY 1976. The statistical summary of registered protocols is given under Report of Total Activities of the Clinical Investigation Service.

Continued support of the BAMC Commander, his administrative staff, the professional medical staff and the Directorate for Clinical Investigation Service enabled this service to continue to perform high quality research work.

Personnel support now includes the Chief (a Biochemist who also administers the laboratory facility), a Computer Programmer, the Editorial Assistant and Secretary, and six enlisted specialists. The Directorate, composed of representatives from the Department of Medicine, Obstetrics and Gynecology, Pediatrics and Surgery, has guided the activities of this service throughout fiscal year 1975 and will continue to do so in the future.

The preparation of this report would have been impossible without the continued, unselfish, competent assistant of Mrs. Dodie Bratten who has been the stabilizing influence in the past year during the change of direction of the service to the Clinical Investigation Service Directorate.

Edward D. Hulton

EDWARD D. HULTON, Ph.D.
Captain, MSC
Chief, Clinical Investigation Service, 14 March 1975

Rudi Ansbacher

RUDI ANSBACHER, M.D.
Colonel, MC
Chief, Clinical Investigation Service, 1 July 1974 to 14 March 1975

REPORT OF TOTAL ACTIVITIES OF CLINICAL INVESTIGATION SERVICE

DURING FISCAL YEAR 1975

A. Objectives

The Clinical Investigation Service was established at Brooke Army Medical Center 9 August 1971 to coordinate clinical investigation activities throughout the hospital complex. It is an independent service directly under the command of the Chief, Professional Services, and operates under the guidance of the Directorate for Clinical Investigations, composed of two members from the Department of Medicine and one each from Obstetrics-Gynecology, Pediatrics, and Surgery, the Clinical Investigation Committee, composed of the chiefs of the various professional departments, and the Human Use Committee, composed of lay personnel.

The Clinical Investigation Service was established to promote, stimulate, coordinate, and provide support for clinical investigation and development activities within Brooke Army Medical Center, including design of experiments, typing and editorial services, and technical liaison with outside facilities.

B. Technical Approach

1. Manpower

a. On March 14, 1975, the Chief, Clinical Investigation Service, due to other pressing clinical duties, was replaced by Captain Edward D. Helton, Ph.D., Biochemist. The latter devotes his full energies to Clinical Investigation Service activities and to the functioning and administration of the laboratory.

b. A Computer Programmer, First Lieutenant Signal Corps, promoted to that rank on 27 April 1975, devotes his time almost exclusively to C-28-73, a cardiology protocol, plus assists other investigators with statistical analyses of their data.

c. The Editorial Assistant and Secretary has devoted all her time to Clinical Investigation Service functions. She keeps a daily running budget for the service and for each individual protocol, orders all supplies and equipment, edits and types all manuscripts for publication prior to final review by a member of the Directorate, and types protocols prior to presentation to the Directorate, Clinical Investigation Committee and Human Use Committee.

d. There are six enlisted specialists now assigned to the service: an E-6, an E-5, two E-4's (one of which was promoted to E-4 on 15 April 1975), and two E-3's who were assigned on 13 November 1974 and promoted to that rank on 16 January 1975. Three of these enlisted specialists are working only in the laboratory facility on Ward 43A.

2. Funding

Table 1.

Expenditures FY 1975

MEDCASE	$ 47,295.00	6 Protocols
	$ 71,585.00	Laboratory
	$118,880.00	
Capital Equipment	$ 1,595.00	2 Protocols
	$ 325.00	Laboratory
	$ 1,920.00	
Consumable Supplies	$ 24,088.00	26 Protocols
	$ 5,492.00	Laboratory
	$ 2,325.00	Contractural Services
	$ 31,905.00	
TDY	$ 3,355.00	
	$156,060.00	

C. Progress

The disposition of protocols registered with the Clinical Investigation Service FY 75 are as follows:

Table 2.

Protocol Disposition FY 75

Registered in:	FY 72	FY 73	FY 74	FY 75	Total
Completed	4	2	12	4	22
Terminated	5	4	2	2	13
Ongoing to FY 76	4	2	22	29	57
TOTAL	13	8	36	35	92

Fifty-seven protocols will be ongoing into FY 76.

During FY 75, 94 manuscripts were cleared through the Clinical Investigation Service, 48 for publication, 13 for satisfaction of residency requirement, and 33 both for satisfying the residency requirement and for publication. Sixty presentations were reviewed and cleared by the Clinical Investiation Service for national and international medical meetings,and most of the material came from protocols registered in the Clinical Investigation Service.

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Hull, J.K.: The Use of Full Thickness Free Skin Grafts in the Treatment of Urethral Strictures in the Male. Presented at the Kimbrough Urological Seminar, San Antonio, Texas, 10-14 November 1974.

Gangai, M.P.: Urologic Leprosy. Scientific exhibit displayed at the meeting of the American Urological Association, May 1975, Miami, Florida.

Hull, J.K.: The Use of Full Thickness Free Skin Grafts in the Treatment of Urethral Strictures in the Male. Presented by COL Mauro P. Gangai to the Texas Medical Association Meeting, May 1975.

PHYSICAL MEDICINE SERVICE

See, D.H. and Kraft, G.H.: Electromyography in paraspinal muscles following surgery for root compression. Arch Phys Med Rehabil 56:80-82, 1975.

See, D.H.: Subacute and Chronic Syndromes. Presented at the University of Texas Health Science Center at San Antonio, 8 June 1974.

See, D.H.: Shoulder Weakness as an Unusual Complication in Burned Patients: Report of 10 Cases. Presented at the annual meeting of American Academy of Physical Medicine and Rehabilitation and American Congress of Rehabilitation Medicine, San Francisco, California, 19 November 1974.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Human Hepatic *in vitro* Metabolism of the Synthetic and Natural Estrogens.

WORK UNIT NO.: C-1-75

PRINCIPAL INVESTIGATOR: Edward D. Helton, Ph.D., Captain, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To correlate the *in vivo* metabolism of 17α-ethynylestradiol and estradiol to the *in vitro* hepatic metabolism and to establish what hepatotoxic effects the potent synthetic estrogen may have upon normal liver function.

TECHNICAL APPROACH

Needle biopsy liver tissue fragments taken from patients for diagnostic purposes are incubated. Using sterile technique, the tissue is cultured with tritium labeled steroids, and following incubation the tissue is thoroughly extracted to remove the steroid metabolites. The extracted tissue is analyzed for the percent of irreversibly bound steroid and the steroid metabolites are purified and identified using Sephadex LH-20 chromatography and gas chromatography-mass spectrometry.

Manpower: E-3 (12 months)

Funding:			
	$2,260.16	Consumable Supplies	FY 1975
	$ 288.00	TDY	FY 1975

PROGRESS

The procedure for incubation has been established and the similarities between the *in vivo* metabolism and in vitro are striking. The system will thus allow meaningful studies of normal and pathological metabolism of estrogen and possibly provide insights into their hepatotoxicity.

Status: Ongoing.

C-1-75 (Continued)

Presented at the Fourth International Congress on Hormonal Steroids, Mexico City, Mexico, 2-7 September 1974.

Helton, E.D., Williams, M.C., and Goldzieher, J.W.: The metabolism of ethynylestradiol in women. Abstract. Endocrinology Supplement to 94, 315, 1974.

Helton, E.D., Williams, M.C., and Goldzieher, J.W.: The metabolism of ethynylestradiol in women. Abstract. Journal of Steroid Biochemistry, 5, 320, 1974.

Williams, M.C., Helton, E.D., and Goldzieher, J.W.: The urinary metabolites of 17α-ethynylestradiol-9α,11ξ-^{3}H in women. Chromatographic profiling and identification of ethynyl and non-ethynyl compounds. Steroids 25(2),229-246, 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: "VD-G Dri DOT" Serological Test for Gonorrhea.

WORK UNIT NO.: C-144-72

PRINCIPAL INVESTIGATOR: David D. Madorsky, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the "Gonosticon Dri-DOT" (formerly "VD-G Dri-DOT") Serological Test for gonorrhea with Thayer Martin cultures and smears in males who present for diagnosis of possible gonococcal urethritis.

TECHNICAL APPROACH

All men presenting for diagnosis of gonorrhea have a Gonosticon Dri-DOT Test and Thayer Martin Culture performed in addition to the smear. The test is performed on serum according to instructions and the end point is read. Results are compared to determine the efficacy of the test.

Manpower: None

Funding: None

PROGRESS

This project has been completed. However, the principal investigator was reassigned before the data could be evaluated, and therefore no results are available.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Antigens in Fire Ant Venom

WORK UNIT NO.: C-41-74

PRINCIPAL INVESTIGATOR: Frank K. James, Jr., Colonel, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, Major, MC
Donald P. Driggers, Captain, MSC

OBJECTIVES

To study the venom and/or its component parts and its effect on selective human volunteers known to be sensitive to the fire ant venom.

TECHNICAL APPROACH

Venom was gathered from the two imported species of ants and prepared for use in specific skin testing on fire ant sensitive patients and controls. Twenty-five fire ant sensitive patients and 15 control patients were studied in detail.

Manpower: None

Funding:

$115.00	Consumable Supplies	FY 1974
$366.00	TDY	FY 1974
$ 75.96	Consumable Supplies	FY 1975

PROGRESS

These studies clearly revealed that sensitivities to the venom were at least 10-20 fold more sensitive than the commercially available fire ant antigen. Passive transfer was accomplished, although there is insufficient information (based on the few patients tested) to make a final comment at this point.

This study will continue gathering: a) a greater patient experience, and b) further studies with both skin testing techniques, passive transfer, and the RAST test.

C-41-74 (Continued)

Status: Ongoing

Presented at the "Imported Fire Ant Research Conference" sponsored by the Department of Agriculture, Gainesville, Florida, 25-27 March 1975.

Presented at the Texas Medical Association Annual Meeting, San Antonio, Texas, 2 May 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Intra-Oral Effects of Different Major Connector Designs for Removable Partial Dentures.

WORK UNIT NO.: C-35-73

PRINCIPAL INVESTIGATOR: Larry D. Campbell, D.D.S., Lieutenant Colonel, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the patient preference of different removable partial denture designs during speaking, swallowing, eating and resting.

TECHNICAL APPROACH

Two metal removable partial denture frameworks, one maxillary and one mandibular, were made for each of twelve dentists. During the seven day study period, the dentures were altered systematically to produce a series of different commonly used designs. Four changes were evaluated on the maxillary framework, and two on the mandibular. Questionnaires were completed by the subjects during and after the study.

Manpower: None

Funding: None

PROGRESS

In general, major connector designs were better tolerated as the systematic alterations progressed. Only one subject selected the full palatal coverage as the preferred maxillary major connector. Four subjects chose the anterior posterior bar, and seven indicated the posterior strap as first choice. Of mandibular major connector designs, three preferred lingual plating while nine selected the lingual bar. None of the subjects endorsed the final modification which required a thickening of the posterior strap.

C-35-73 (Continued)

Conclusions: The partial denture design does influence the ultimate success of patient treatment. Patient acceptance and satisfaction depend upon logical and purposeful placement of all denture borders. Ease of speech, mastication, swallowing, and general comfort are affected by design. This investigation points out that removable partial denture patients show a definite preference for what is being placed into their mouths. The final design criteria must also depend upon multiple mechanical and biological principles encountered with each patient. The dentist prescribing prosthodontic treatment will have a solid basis for partial denture prescription and design if the biomechanical considerations can be tempered with the clinical preferences of the patient.

Status: Completed.

Submitted to the Journal of Prosthetic Dentistry for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Acceptability of Lateral Interocclusal Records by the Whip-Mix Articulator.

WORK UNIT NO.: C-25-74

PRINCIPAL INVESTIGATOR: L. James Bell, D.D.S., Major, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate clinically the use of lateral interocclusal records in setting the condylar elements of the Whip-Mix articulator; particularly to evaluate the acceptability of these records by the articulator.

TECHNICAL APPROACH

Twenty-five subjects were chosen at random. The only qualification necessary was an optimum state of oral health. Two maxillary and one mandibular alginate impressions were made on each subject. Two interocclusal record bases were constructed for each subject, placed in the subject's mouth and observed for accuracy of fit and possible tissue contact. The interocclusal record, upon examination by the investigator, had to show the following in order to be usable: (a) no contact between the record and the soft tissue, and (b) no contact between the teeth and the record base. The split-cast technique was used in the mounting procedure.

Manpower: None

Funding: $385.30 Consumable Supplies FY 1974

PROGRESS

Of the fifty condylar settings obtained, ten were not accepted by the articulator. All of the interferences preventing the instrument from being adjusted occurred on the working condyle side. Seven registrations were impeded by the posterior wall of the condylar housing and three by the superior wall. Of those accepted

C-25-74 (Continued)

the range of adjustability of this instrument varied from 0° to 25° for the medial guide, and from 15° to 70° on the condylar guide.

In spite of the above observations, this instrument proved itself to be a useful tool in the dental armamentarium for the following reasons:

1. The intercondylar width is semi-adjustable.
2. The face-bow transfer is efficient and accurate.
3. The instrument increases the dentist's diagnostic range especially in evaluating working condylar direction.
4. It is a well constructed and durable instrument.

Status: Completed.

Submitted to the Journal of Prosthetic Dentistry for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A New Anesthetic for Use in Oral Surgery

WORK UNIT NO.: C-33-74

PRINCIPAL INVESTIGATOR: John A. Nespeca, D.D.S., Major, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine onset of action, duration, potency, side effects, and other distinguishing features of Bupivicaine Hydrochloride (marcaine) in oral surgical procedures.

TECHNICAL APPROACH

Two hundred sixty-two patients were treated using randomly selected local anesthetic agents--Bupivacaine .25% and .5% with or without epinephrine and Lidocaine 2% with or without epinephrine.

The agents were evaluated and compared by recording four specific clinical parameters: (1) Duration; (2) Onset; (3) First Pain; and (4) Total Medications.

Manpower; None

Funding: $992.69 Consumable Supplies FY 1974

PROGRESS

Bupivacaine, .5% and .25% without epinephrine, was very difficult to use. The onset was prolonged and the anesthetic effectiveness was questionable. The agents without epinephrine were therefore abandoned from the remainder of the study. Lidocaine without epinephrine was likewise deleted from the study.

One way analysis of variance indicated a significant difference among mean time of onset for the three agents. T-test revealed that both

C-33-74 (Continued)

strengths of Marcaine required a longer time of onset than Xylocaine. There was, however, no significant difference of onset between the two strengths of Marcine.

The onset of first pain when compared showed significant difference among the three medications. T-tests showed significant differences when comparing Marcine to Xylocaine. There was also a significant difference with Marcaine .25% compared to Marcaine .5% ($p<.02$).

The total postoperative analgesics had a significant difference among the three agents. T-tests showed a greater number of postoperative medications were required with Xylocaine than with either of the two Marcaines ($p<.001$). The difference between the two strengths of Marcaine was not significant.

Marcaine appears to be a safe local anesthetic quite effective for long extended durations. Patients require less analgesic support during their early postoperative period and tolerate the long duration of anesthesia without complication. Marcaine would be indicated in those cases where severe postoperative pain is unavoidable.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Histologic Examination of Plaster Sealed Osseous Coagulum Grafts.

WORK UNIT NO.: C-5-75

PRINCIPAL INVESTIGATOR: James J. Lane, D.D.S., Colonel, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if plaster placed over osseous coagulum grafts prevents the proliferation of epithelium into the osseous defect, and allows connective tissue to form a new attachment with the root surface.

TECHNICAL APPROACH

Five patients requiring extraction of their remaining maxillary teeth for the insertion of an immediate maxillary denture will have osseous coagulum grafts placed in the base of the infrabony pocket. A plaster seal will be placed in the coronal portion of the bony defect to the alveolar crest of one tooth. Fourteen days later, a block section will be taken of the adjacent soft and hard tissue of the grafted surface of the tooth for histologic examination. At this time the remaining teeth will be removed and immediate maxillary dentures will be inserted.

Manpower: None

Funding: None

PROGRESS

This project is terminated due to transfer of principal investigator.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Oral Transplants of Freeze-Dried Allografts.

WORK UNIT NO.: C-12-75

PRINCIPAL INVESTIGATOR: John H. Moyer, D.D.S., Major, DC

ASSOCIATE INVESTIGATORS: James J. Lane, D.D.S., Colonel, DC

OBJECTIVES

To determine whether freeze-dried bone allografts can be used in one, two and combined one and two wall oral bony defects, with predictable results.

TECHNICAL APPROACH

The surgical site will be exposed via a buccal and lingual full or partial thickness mucoperiosteal flap. Intraosseous defects will be recontoured and one wall or two wall bony defects will be prepared by removing the cortical place within the defect. The freeze-dried allograft material will be mixed with sterile saline to a paste-like consistency and packed in and around the existing bony defect. The patients will be recalled one year post-grafting to re-open the operative site for evaluation and additional surgical intervention as indicated.

Manpower: None

Funding: None

PROGRESS

Approximately 20 of these grafts have been done, and none are one year postoperative at which time we are to reenter.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Design Alterations Upon Abutment Tooth Mobility with Removable Partial Dentures.

WORK UNIT NO.: C-28-75

PRINCIPAL INVESTIGATOR: John McCartney, D.D.S., Major, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine via intraoral procedures whether alterations in design of the prosthesis have any effect upon the amount and direction of force transmitted to the abutment tooth when a bilateral extension removable partial denture is subjected to forces upon its distal extension bases.

TECHNICAL APPROACH

A bilateral distal extension removable partial denture will be made abutting with teeth #21 and 27. Teeth #21 and 27 will receive restoration via full crown castings. The partial denture will have five removable components to allow for variation of clasping and comparisons of transmitted forces to abutments. Tooth #21 will serve as the test abutment, movements buccolingually and mesiodistally to be measured by pressure gauges attached to a fixed platform attached to teeth #23-26. Alterations in the master framework will give information as to the relative influence of its component parts.

Manpower: None

Funding: None

PROGRESS

As of this date, teeth #21 and 27 have been restored, the master frame and all inserts have been adjusted in the mouth, and the function of all testing apparatus has been completed to meet clinically observable requirements.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Topical Vitamin A Acid in Lamellar Ichthyosis.

WORK UNIT NO.: C-39-72

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., Lieutenant Colonel, MC

ASSOCIATE INTESTIGATORS:

OBJECTIVES

To evaluate and utilize an effective topical preparation in a selected number of dermatoses which are generally unresponsive to other therapeutic modalities.

TECHNICAL APPROACH

Preparations will be applied topically to the affected area initially t.i.d. to the end point of cutaneous irritant dermatitis. Frequency of application is adjusted to several schedules, depending on response. Patients will be closely followed with periodic medical photographs and skin biopsies when indicated.

Manpower: None

Funding: None

PROGRESS

Three patients have undergone long term use of topical Vitamin A acid to control the thick scales produced by ichthyosis. One patient recently was discontinued from the study due to loss of military eligibility. Two other patients continue to show good control of their skin condition and no adverse effects to the drug.

Since the medication is not commercially available, the study has been terminated.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Application of the Fluorescent Antibody Technique to the Investigation of Various Dermatoses.

WORK UNIT NO.: C-44-72

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To demonstrate the presence or absence of skin auto antibodies or antibodies in the epithelium or sera of patients with a variety of bullous and nonbullous dermatoses.

TECHNICAL APPROACH

Application of standard fluorescent techniques for direct and indirect immunofluorescense of skin biopsies.

Manpower: None

Funding:

$200.00	Consumable Supplies	FY 1973
$277.90	Consumable Supplies	FY 1974

PROGRESS

A total of 125 skin samples and 20 renal biopsies were processed and run three times for control checks. Forty-five of the skin samples were from outlying posts using our special fixative. Thirty-two skin biopsies were positive for basement membrane fluorescence, 12 biopsies revealed vascular fluorescence, and other positive indirect tests were recorded.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Use of Hydroxyurea in Patients with Disabling Psoriasis

WORK UNIT NO.: C-58-72

PRINCIPAL INVESTIGATOR: Bobby L. Limmer, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the therapeutic efficacy and side effects of the anti-metabolite hydroxyurea in patients with disabling and incapacitating psoriasis with or without arthritis.

TECHNICAL APPROACH

With adequate documentation of severe psoriasis and normal laboratory data, patients were started on 200 mg of hydroxyurea at various time intervals depending on severity of disease and response to previous medication.

Manpower: None

Funding: None

PROGRESS

This protocol has been terminated due to transfer of principal investigator.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Alcohol Withdrawal and Sleep Deprivation in the Production of Seizures.

WORK UNIT NO.: C-126-72

PRINCIPAL INVESTIGATOR: Carl H. Gunderson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Thomas L. Feher, M.D.
Peter B. Dunne, M.D.

OBJECTIVES

Comparison of alcohol withdrawal and sleep deprivation in precipitating seizures.

TECHNICAL APPROACH

Data has been collected.

Manpower: None

Funding: None

PROGRESS

No progress has been made since last report; therefore, the project is terminated.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: EEG and Other Correlates of Sleep Deprivation Seizures.

WORK UNIT NO.: C-127-72

PRINCIPAL INVESTIGATOR: Carl H. Gunderson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Thomas L. Feher, M.D.; Peter B. Dunne, M.D.; E. Liske, M.D.

OBJECTIVES

To compare sleep deprivation EEG's of patients who have had seizures following sleep deprivation and those who have not.

TECHNICAL APPROACH

Data has been collected.

Manpower: None

Funding: None

PROGRESS

No progress has been made since last report; therefore, the project is terminated.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Minocin Treatment of Gonorrheal Urethritis.

WORK UNIT NO.: C-129-72

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To ascertain the best therapeutic dose of Minocin for treatment of acute gonorrheal urethritis in outpatients.

TECHNICAL APPROACH

Evaluation of Minocin capsules in the treamtnet of gonorrheal urethritis in adult males. Two dosage schedules are utilized with the drug randomized so that the physician does not know what dosage the patient will be receiving.

Gram stains, cultures, and VD-G Dri-Dot test will be done pre-therapy, at 48 hours, and 7 days post-therapy. Blood will be drawn to determine serum levels of Minocin. These samples will be evaluated by Lederle Laboratories.

Manpower: None

Funding: None

PROGRESS

Two hundred patients were entered into the study group with approximately 100 patients completing follow-up evaluations. Data is presently being analyzed.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Port Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Study of Tobramycin

WORK UNIT NO.: C-147-72-1

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the clinical efficacy of the aminoglycoside tobramycin in the treatment of serious gram-negative infections.

TECHNICAL APPROACH

Hospitalized patients were admitted to the study with the following indications. 1. Urinary tract infection; 2. Gram negative pneumonia; 3. Gram negative sepsis and bacteremia; 4. Severe surgical wound infections; 5. Neonatal sepsis with or without meningitis. Routine hematological, urinalysis and urine culture, liver function and renal function studies were performed before, during and following therapy. Dosage would not exceed 6 mg/kg/24 hours and serum concentrations were determined at three points during the course.

Manpower: None

Funding: None

PROGRESS

Twenty-eight patients with infections due to sensitive gram-negative organisms have been treated. Eighteen had urinary tract infection as determined by colony counts of greater than 100,000 colonies of gram negative organisms on multiple clean catch or catheterized urine specimens. Of the remaining 10 patients, 5 had gram negative bacteremia and 5 had significant soft tissue infections. The average dose ranged between 3 to 5 mg/kg administered in divided doses every 8 hours.

C-147-72-1 (Continued)

At these dosage ranges levels of 6 to 10 micrograms/ml 1 hour following infusion were obtained. All levels were below those previously established for oto or nephrotoxicity and no toxicity was noted in the patient groups. All patients had a satisfactory clinical response although one patient developed a urinary tract infection secondary to Providencia stuartii following therapy with Tobramycin. A second patient with Pseudomonas urinary tract infection presented a problem of rapid Tobramycin elimination. No allergic manifestation or toxicity was noted and when compared to Gentamicin in a randomized fashion, there was a suggestion that less toxicity occurred in the Tobramycin treated patients.

A portion of this material was presented before the Fourteenth Interscience Conference on Antimicrobial Agents and Chemotherapy in San Francisco, California.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Neurology Workload Project.

WORK UNIT NO.: C-149-72

PRINCIPAL INVESTIGATOR: Carl H. Gunderson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine and compare workload of Neurology Services at Class I and Class II hospital and compare these with comparable civilian studies.

TECHNICAL APPROACH

All patients seen in Neurology Services of Brooke Army Medical Center, Darnall Army Hospital, and Reynolds Army Hospital are being registered for a two week period. Information will be transferred to punch cards and card sorted. A second two week period will be studied at a later date and the data handled similarly. The two samplings will be compared for internal consistency. If they are internally consistent, they will be combined and the comparison made between the various hospitals and the civilian population.

Manpower: None

Funding: None

PROGRESS

No progress has been made since the last report; therefore, the project is terminated.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Determination of Patch Test Reaction Time

WORK UNIT NO.: C-5-73

PRINCIPAL INVESTIGATOR: Daniel B. Clarke, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the significant patch test reaction times and locations with known allergens included in a standard patch test screening tray.

TECHNICAL APPROACH

Photographic documentation of patch test response at various times and body locations on known positive patch test reactor.

Manpower: None

Funding: None

PROGRESS

Terminated due to transfer of principal investigator.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Cyproheptadine in the Management of Patients with Idiopathic Chronic Immunic Complex-Induced Glomerulonephritis: A Controlled, Double-Blind Cooperative Study.

WORK UNIT NO.: C-27-73

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Daniel A. Nash, Jr., M.D., Major, MC
David B. Olin, M.D., Major, MC

OBJECTIVES

This study was designed to arrest chronic complex-induced glomerulonephritis in humans by preventing antigen-antibody complex deposition in the capillary loops in the glomeruli.

TECHNICAL APPROACH

Manpower: None

Funding: None

PROGRESS

Terminated due to lack of patients meeting protocol criteria.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Simultaneous Determination of Instantaneous Aortic Flow, High Fidelity Intracardiac Pressures, Intracardiac Phonocardiography, Echocardiographic Dimensions, and Derived Indices in Man.

WORK UNIT NO.: C-28-73

PRINCIPAL INVESTIGATOR: Joseph P. Murgo, M.D., Major, MC

ASSOCIATE INVESTIGATORS: George M. McGranahan, Jr., M.D., Colonel, MC
Hal A. Martin, M.D., Major, MC
James P. Dorethy, M.D., Major, MC

OBJECTIVES

1. To develop new techniques in cardiac catheterization, especially in the area of multi-solid state sensor catheters including high fidelity pressure sensors and electromagnetic flow meters. To utilize high speed biplane angiography and external echocardiography in conjunction with such techniques.

2. To utilize these techniques to define sophisticated parameters of ventricular function in patients with various cardiac diseases.

3. To develop specialized computer-assisted analyses of the data derived from such studies.

4. To quantitate left ventricular hydraulic output power.

5. To measure aortic and pulmonary artery input impedance by Fourier analysis and to determine the effect of changing physiologic states upon the impedance.

6. Detailed description of multiple specific objectives are to be found in the original protocol.

TECHNICAL APPROACH

All patients (Adult) coming to routine right and left heart catheterization are evaluated in the usual manner by a cardiac fellow prior to catheterization. This evaluation includes strip chart echocardiography to determine the patient's suitability for certain aspects of the protocol.

C-28-73 (Continued)

During catheterization, a special custom designed triple-tip right-sided catheter is introduced into the right heart such that simultaneous high fidelity pressures are measured from the pulmonary artery, right ventricle and right atrium. A second, more conventional catheter is also introduced into the pulmonary artery for purposes of blood specimen withdrawal, etc. The left heart is catheterized using a multiple sensor custom-designed catheter such that high fidelity left ventricular and left atrial pressures are measured as well as ascending aortic electromagnetic flow velocity. Patients are studied during both rest and supine exercise; and in some protocols, depending on the patient's disease, they are studied utilizing a variety of other stresses. Following the collection of hemodynamic data, the patients undergo external echocardiography while simultaneously measuring pressures and flows, and the study is terminated using biplane ventricular angiography and coronary arteriography if indicated. All patients also undergo an aortic root angiography for the purposes of determining aortic root diameter which is necessary to convert flow velocity to flow itself. An on-line Honeywell 316 computer presently exists in the laboratory and is capable of sampling all pressures, electrocardiograms and flow simultaneously. This computer will print out the results of all of these parameters immediately, simplifying the data analysis immensely. Specially designed research programming for the computer was added: electro-mechanical and flow time intervals and hydraulic output power are calculated and displayed. A Fourier analysis program used to compute impedance will soon be implemented. Angiograms and echocardiograms are analyzed using Hewlett Packard programmable calculators and digitizer. The newly acquired patient data storage system (mass memory) is being used to gather statisical data on a scale not previously possible.

Manpower: 2LT (9 months)
1LT (3 months)
E-4 (12 months)

Funding:

$33,654	MEDCASE	FY 1975
$ 129.76	Consumable Supplies	FY 1975
$ 1,018.00	TDY	FY 1975
$29,354.25	MEDCASE	FY 1974
$ 862.40	Capital Equipment	FY 1974
$43,573.00	Consumable Supplies (Contractural Svc)	FY 1974
$ 1,195.68	TDY	FY 1974
$43,300.00	PEMA	FY 1973

C-28-73 (Continued)

PROGRESS

Since last year's report, significant progress has been made in the development and implementation of research programming for the catheterization laboratory computer. Blood flow in the ascending aorta has been carefully studied, and measurements of peak values, duration and timing of the flow pulse have been made in more than fifty patients. The Echocardiogram vs. Angiogram study has been expanded to thirty-seven patients. New studies to measure hydraulic power and ventricular geometry are under way. Algorithms suitable for computing frequency spectra and complex impedance in the vascular system have been developed and will be implemented.

"The Dynamics of Left Ventricular Ejection in Man Utilizing New Techniques in Cardiac Catheterization." Presented at the Cardiovascular Research Seminars, University of Texas Health Science Center, San Antonio, Texas, September 1974.

"The Dynamics of Left Ventricular Ejection Utilizing New Techniques in Cardiac Catheterization and Continuous Indices of Ventricular Diameter and Volume Utilizing External Echocardiography." Presented at Special Research Seminar, School of Aerospace Medicine, Brooks Air Force Base, San Atnonio, Texas, October 1974.

"The Ejection Characteristics of IHSS." Presented as part of a panel discussion of the Medical and Surgical Management of Idiopathic Hypertrophic Subaortic Stenosis, 47th Scientific Sessions, American Heart Association, Dallas, Texas, November 1974.

"A Simple Technique for Obtaining Continuous Left Ventricular Diameter and Derived Indices from Strip Chart Echocardiography." Presented at 47th Scientific Sessions of the American Heart Association, Dallas, Texas, November 1974.

Invited lecture to the Laennec Society, entitled "Instantaneous Pressure-Flow Dynamics: Genesis of Heart Sounds and Murmurs". 47th Scientific Sessions of the American Heart Association, Dallas, Texas, November 1974.

"Transmural Myocardial Infarction without Demonstrable Coronary Occlusion." Presented at the 47th Scientific Sessions of the American Heart Association, Dallas, Texas, November 1974.

Invited lecture "Biomedical Instrumentation," presented to the Bio-Engineering Section, University of Texas Health Science Center, San Antonio, Texas, December 1974.

C-28-73 (Continued)

Participation in the Cardiac Clinic entitled "Modern Methods in Evaluation of Cardiac Disease" held in conjunction with the annual sessions of the American College of Cardiology, February 1975.

a. Contribution of High-Fidelity Monometry and Flow Velocity Analysis.
b. Contribution of Computers to the Cardiac Catheterization Laboratory.

Fireside Panel as part of the Annual Sessions of the American College of Cardiology, entitled "Advanced Techniques for Evaluating Cardiovascular Function" February 1975.

"New Techniques in Cardiac Catheterization - The Advantages of Multisensor Catheters." First prize paper presented to the National Society of Cardiopulmonary Technologists, Miami, Florida, May 1975.

Altobelli, S.A. and Murgo, J.P. A simple technique for obtaining continuous left ventricular diameter and derived indices from strip chart echocardiography. Circulation, Supp III, 50:102, 1974.

McGranahan, G.M., Murgo, J.P. and Dorethy, J.F. Transmural myocardial infarction without demonstrable coronary occlusion. Circulation, Supp III, 50:595, 1974.

Dorethy, J.F., Altobelli, S.A. and Murgo, J.P. Right ventricular-pulmonary artery impulse gradients in man during rest and exercise. Circulation, Supp III, 50:884, 1974.

Martin, H.A., McGranahan, G.M. and Murgo, J.P. The ejection dynamics of IHSS in the presence and absence of gradients. Circulation, Supp III, 50:931, 1974.

Murgo, J.P. The dynamics of left ventricular ejection in patients with normal hemodynamics. Circulation, Supp III, 50:936, 1974.

Murgo, J.P. Ventricular ejection mechanics, how the left ventricle works. Submitted to Circulation to be published in a special supplement of a three day symposium entitled "Physiologic Principles of Heart Sounds and Murmurs 1974" held in Pittsburgh, Pa., April 1974 and sponsored by the American Heart Association and the University of Pittsburgh.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Skin Window Studies in Trichophyton Hypersensitivity.

WORK UNIT NO.: C-39-73

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the type of cellular response in patients with tinea pedis as revealed by the skin window technique utilizing trichophyton antigen.

TECHNICAL APPROACH

Apply glass cover slips under occlusion over skin test site on forearms of patients with chronic tinea pedis. Purpose is to evaluate the basophile and eosinophil response to fungal antigenic stimulation as measured by the skin window technique.

Manpower: None

Funding: None

PROGRESS

There were no statistical differences between groups.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Calcium Metabolism During Acute Renal Insufficiency.

WORK UNIT NO.: C-40-73

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Daniel A. Nash, Jr., M.D., Major, MC

OBJECTIVES

To determine the mechanism of hypercalcemia seen in some cases of acute renal insufficiency.

TECHNICAL APPROACH

All patients with acute renal failure will be surveyed. They will be divided into two groups in an alternate manner. The usual dietary and chemotherapeutic modalities for treating acute renal failure will be employed. Hemodialysis and peritoneal dialysis will be reserved for those patients who are uremic or in whom fluid and potassium balance cannot be controlled by conservative means. Serum phosphorus will be maintained below 6 mg% in one group, and the second group will go untreated. For those able to eat, 1000 mg calcium and 1500 mg phosphorus will be offered. Percutaneous renal biopsies will be examined by light microscopy, electron microscopy, and immunofluorescent microscopy. Patients with acute renal insufficiency will have three 6-hour dialyses a week. Serial determinations will be done to detect any manifestations of hypercalcemia. In addition, serum parathyroid hormone will be measured and an attempt will be made to correlate the hypercalcemia that is frequently seen following acute renal insufficiency with increased parathormone secretion.

In those patients developing hypercalcemia in the diuretic phase, efforts will be made to suppress parathormone secretion by calcium infusion or phosphorus depletion. When possible weekly eye examination will be performed to document early metastatic calcification. Skin biopsies will be analyzed for calcium.

C-40-73 (Continued)

Manpower: None

Funding: None

PROGRESS

To date no patient has been entered into this protocol.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Association of Immune Complex Renal Disease in Hepatitis.

WORK UNIT NO.: C-41-73

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Gerald A. Hiatt, M.D., Major, MC

OBJECTIVES

To determine the incidence of immune complex glomerulonephritis in acute hepatitis.

TECHNICAL APPROACH

All patients with hepatitis associated antigen positive hepatitis will be studied. Any patient who demonstrates abnormalities of renal function by depressed creatinine clearance, abnormalities of urinary sediment or proteinuria will be considered for renal biopsy. Biopsy will be submitted for light, electron, and immunofluorescence microscopy. Those patients demonstrating an immune complex type of nephritis will be further studied for the presence of hepatitis associated antigen antibody complexes in the renal glomerulus.

Manpower: None

Funding: None

PROGRESS

To date, 13 patients and 76 urine studies have been performed. Evaluation of the material to date indicates that no satisfactory data will be gathered from this particular approach to immune complex glomerulonephritis. Therefore, the protocol is terminated.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: In vitro Susceptibility of Candida and Torulopsis Species Isolated from Hospitalized Patients to Nystatin, 5-Fluorocytosine and Amphotericin B.

WORK UNIT NO.: C-2-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare in vitro susceptibility of Candida and Torulopsis species isolated from patients who are receiving broad spectrum antibacterial or antifungal agents against similar species isolated from hospitalized patients who are not receiving such agents.

TECHNICAL APPROACH

One-hundred-one isolates were tested against Nystatin, Amphotericin B and 5-fluorocytosine. Strains isolated from patients were studied. Sensitivity testing was done by tube dilution technique, carried out in duplicate for each isolate.

Manpower: E-5 (4 months)

Funding: None

PROGRESS

Since the last progress report these 101 strains have also been tested to Candicidin, a polyene antifungal agent. All of the strains tested were sensitive at 0.195 mcg/ml or less. There was a 16% resistance to 5-fluorocytosine; however, all organisms were sensitive to both Amphotericin B and Nystatin. When the degree of sensitivity with the three polyene antifungal agents Amphotericin B, Nystatin and Candicidin were

C-2-74 (Continued)

compared, there was a suggestion of dissimilarity with certain strains being sensitive to one agent at very high MIC's and to one of the other agents at very low MIC's. This suggests the potential of stepwise resistance and further evaluation of this potential resistance with comparison to a content of ergosterol within each of the strains is planned.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Physiologic Evaluation of Pulmonary Status in Patients Undergoing Renal Dialysis.

WORK UNIT NO.: C-4-74

PRINCIPAL INVESTIGATOR: William W. Burgin, Jr., M.D., Lieutenant Colonel, MC
ASSOCIATE INVESTIGATORS: Robert B. Blumer, M.D., Lieutenant Colonel, MC
Richard H. Merrill, M.D., Major, MC

OBJECTIVES

To evaluate the pulmonary function in renal dialysis patients both pre- and post dialysis, to better ascertain the physiologic changes which take place in the lung.

TECHNICAL APPROACH

Twelve patients in the dialysis program at Brooke Army Medical Center have been evaluated pre- and post dialysis as to the effect dialysis has on pulmonary function capability and oxygen carrying capacity of the blood.

Manpower: None

Funding: None

PROGRESS

Generally, the studies are as predicted in that the patients who undergo pulmonary function evaluation before dialysis tend to do more poorly than those same patients after undergoing dialysis. The study is presently proceeding more slowly because of discrepancies in the 2-3 DPG studies, when compared with the P_{50} values before and after dialysis. These spurious data must be explained before this investigation is deemed reportable.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Study of Aminoglycoside Antibiotic BB-K8.

WORK UNIT NO.: C-8-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To evaluate therapeutic effectiveness of BB-K8 in the treatment of hospitalized adult patients with infections caused by susceptible pathogens.

2. To establish an optimal therapeutic dosage schedule for BB-K8 which is safe and effective.

3. To establish a side effect profile for the drug.

4. To obtain information on the clinical pharmacology of the drug in diseased patients.

TECHNICAL APPROACH

BB-K8 is given by deep intramuscular injection at the appropriate site at a dose not to exceed 7.5 mg/kg every 12 hours. Each patient and his clinical record will be evaluated twice a day throughout the course of drug therapy. Patients with urinary infections will have repeat urine culture and colony counts at 48 to 72 hours after initiation of therapy. Each patient will be followed by daily urinalysis with microscopic examination; BUN and creatinine determinations will be performed every 48 hours throughout the period of drug administration. Audiograms will be performed on the 3rd, 6th and 10th days of therapy. Appropriate specimens will be forwarded to Bristol Laboratories for determination of BB-K8 concentrations. Appropriate post treatment cultures will be obtained at the conclusion of BB-K8 therapy. Repeat chest x-rays will be obtained and patients with septicemia will have post treatment blood cultures.

Manpower: E-5 (2 months)

Funding: $51.30 Consumable Supplies FY 1974
$82.74 Consumable Supplies FY 1975

C-8-74 (Continued)

PROGRESS

Preliminary laboratory investigation documented that 75% of gram negative organisms resistant to standard aminoglycoside anbiotics were sensitive to BB-K8. This preliminary evaluation demonstrated that the Kirby-Bauer zone diameter site did not necessarily correlate with the tube dilution sensitivity technique in determining susceptibility or resistance. One patient with osteomyelitis secondary to Serratia marcescens has been treated. There was no evidence of renal or auditory toxicity and during the course of therapy cultures reverted to negative. The draining sinus healed and the patient was discharged from the hospital. While it is not to be assumed that cure of chronic gram negative osteomyelitis occurred, it was evident that a satisfactory clinical response with shortening of the hospital stay had been the result of this patient's treatment. Further investigations are planned.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Clinical Study of Intravenous Veracillin (Sodium Dicloxacillin).

WORK UNIT NO.: C-9-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Barry Sieger, M.D., Major, MC
Preston Cannady, M.D., Major, MC

OBJECTIVES

To determine efficacy and safety of intravenous veracillin when used in the treatment of infections due to susceptible organisms.

TECHNICAL APPROACH

Patients were included after giving appropriate informed consent when evidence of an infection due to a susceptible organism was present. Laboratory evaluation included a complete blood count, differential and platelet estimation, liver function test, renal function tests, urinalysis as well as serum creatinine and BUN. All examinations were performed within 24 hours prior to starting therapy and every fifth day of therapy. At the conclusion of therapy, repeat laboratory evaluation was carried out. Cultures from the appropriate site were repeated during and after cessation of therapy. Dicloxacillin was used in the standard dose of 1000 mg q6H IV in severe infections or a dose of 250 to 500 mg q6H IV for minor wound or soft tissue infections. Serum killing levels were determined using standard techniques with patient's serum.

Manpower: E-5 (4 months)

Funding: None

PROGRESS

Since the institution of this protocol, three patients were treated with intravenous Veracillin The indications for therapy had been extensive cellulitis in two and abscess formation in one. Clinical

C-9-74 (Continued)

response occurred in all three patients, however appeared to be delayed in two of three patients. No allergic manifestations or drug toxicity were noted. Initial information in relationship to the drug suggested that prolonged high blood levels might be present following the intravenous use. This was not confirmed in the three patients studied to date. Peak serum levels of 7 to 10 micrograms occurred 1 hour after infusion. Levels obtained 5 hours post infusion had fallen to 2 mcg/ml or less. It was therefore felt that the antibiotic should be administered more frequently, perhaps every four hours. In discussing these problems with the manufacturer it became apparent that intravenous Veracillin while perhaps effective was of limited value and a decision was made to cease manufacture of this drug, therefore the study was discontinued.

The results of interest in the study prompted persistent investigation of significant Staphylococcal infections and as a secondary result two abstracts have been submitted to the Fifteenth Interscience Conference on Antimicrobial Agents and Chemotherapy in Washington, D.C. The first abstract is a review by Dr. Barry E. Sieger, Assistant Chief of Infectious Disease, of 40 cases of Staphylococcemia which have been seen over a two year period in the Institute of Surgical Research. Fifty-two and a half percent of these involved Methicillin resistant staphylococci where this was defined by a mean inhibitory concentration of 12.5 micrograms/ml after an overnight incubation at 37°C, in a standard tube dilution assay. Resistance developed during the treatment of 7 of these 21 strains with at least a 2 tube increase in the mean inhibitory concentration. Clinically there was little difference between the pattern of diseases shown by the resistant or sensitive organisms. Apart from a wound infection in 45%, pneumonia was the most common tissue infection (42.5%) followed by suppurative phlebitis (22.5%), myocarditis (17.5%), and endocarditis (12.5%). Simultaneous bacteremia with other organisms particularly gram negative rods was found to be very common. Staphylococcemia was observed with a mean of 14.3 days following admission to the Burn Unit and invariably followed colonization or infection of other body sites. Overall mortality rate was 72.5%. Response to antibiotic therapy was obscured by the coexistence of multiple diseases and retarded by the presence of undrained abscesses in some cases. A similar number of cases are known to have existed over a preceding two year period. This was considered to be the largest outbreak of staphylococcemia due to Methicillin resistant staph at a single Center heretofore described in the United States.

As a result of the evaluation of this problem with Staphylococcemia particularly in relationship to the endocarditis, therapy with Vancomycin was evaluated. The suggestion of rapid antibiotic clearance

C-9-74 (Continued)

in burn patients coupled with the occurrence of several cases of endocarditis due to methicillin resistant Staph Aureus prompted the study of the Vancomycin kinetics in burn patients. Vancomycin was administered in 15 minute infusions every 6 hours with serum Vancomycin levels by bioassay measured prior to infusion at 1/2, 1, 2, 3, 4, 5, and 6 hours from the start of infusion. Six hour catheterized urines were obtained for Vancomycin and Creatinine. The following results were obtained: In patient #1, following a dose of 500 mg, a baseline Vancomycin level of 7.2 microgram/ml, a peak level of 20 microgram/ml with a T½ of 1.7 hrs 483 mg were excreted in 6 hours in the urine. Creatinine clearance was 107 cc/minute. Patient #2 received a dose of 350 mg. His baseline level was 3.7 microgram/ml with a peak serum level of 23.5 microgram/ml and a half-life of .9 hours. 314 mg were recovered in the urine within 6 hours. Creatinine clearance was 99.8. Patient #3 received a dose of 500 mg. Baseline levels were 17.5 with peak serum levels of 40 microgram/ml. T½ was 2.1 hours and 370 mg were recovered in the urine in the first 6 hours of treatment. Creatinine clearance was 49.6. Patient #4 received 500 mg at a baseline level of 13 with a peak of 25.7 microgram/ml and a half-life of 1.7 hours. Urinary concentrations and creatinine clearance were unobtainable. The final patient received 500 mg having a serum baseline level of 4.3 and a peak of 39 microgram/ml and a half-life at 1.5 hours. These results indicate that Vancomycin half-life is not unusually short in burn patients and standard dosage intervals produce adequate drug levels. Monitoring of Vancomycin levels especially in patients with decreased renal function appears to be indicated. Further evaluation of these findings are in order.

Status: Completed

"Vancomycin Kinetics in Burn Patients." Submitted for consideration for presentation at the Fifteenth Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington D.C., September 1975.

"Methicillin Resistant Staphylococci (MRS) in a Burn Unit: Clinical Aspects." Submitted for consideration for presentation at the Fifteenth Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington D.C., September 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Class II Clinical Study of Ticarcillin (BRL 228)

WORK UNIT NO.: C-10-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Barry Seiger, M.D., Major, MC
Preston Cannady, M.D., Major, MC

OBJECTIVES

To evaluate the effectiveness and safety of various dosages of ticarcillin in the treatment of infections in hospitalized patients where those infections are the result of susceptible organisms: E. coli, Proteus mirabilis, Proteus morganii, Proteus rettgeri, Proteus vulgaris, Providencia stuartii, Pseudomonas aeruginosa, Mima, Herellea, Enterobacter aerogenes, Enterobacter cloacae, Citobacter freundii, and Serratia marcescens.

TECHNICAL APPROACH

Patients with infections secondary to sensitive gram negative rods, after receiving informed consent, were treated with intravenous Ticarcillin at a dose of 300 mg/kg/24 hours. CBC, platelet and bleeding time, SMA-18, urinalysis, urine culture and susceptibility testing was done when indicated. All examinations were performed prior to starting therapy, during therapy and 24 hours following cessation of therapy. Antibiotic levels were obtained. Using a random number table, patients were randomized either to a Ticarcillin category or a Carbenicillin category.

Manpower: E-5 (2 months)

Funding: $262.86 Consumable Supplies FY 1975

PROGRESS

Initially three patients were treated with intravenous Ticarcillin for treatment of urinary tract infections with Pseudomonas aeruginosa. In all three cases prompt clinical response occurred and no

C-10-74 (Continued)

adverse reactions were noted. Blood levels between 40 to 80 mcg/ml with urinary levels of 2000 to 4000 mcg/ml were obtained. Subsequently an additional eight patients have been treated in randomized fashion, four have received Carbenicillin and four have received Ticarcillin, at the same dosage regimen initially used. During this phase of testing, phlebitis developed in three of the four patients treated with Ticarcillin and a skin rash developed in the fourth. Because of this extraordinary high incidence of adverse side effects further study was suspended until a new lot of antibiotic had been obtained. This antibiotic is currently available and with changes in the dosage regimen the testing will be undertaken.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Transfusion - Efficiency and Methods to Improve Current Results in Thrombocytopenia Patients.

WORK UNIT NO.: C-16-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To improve the quality of platelet transfusions in thrombocytopenic patients and platelet transfusion complications.

TECHNICAL APPROACH

Evaluation of methods of identifying platelet antibodies by several methods including Serotonin release, platelet factor III, immuno-injury, and platelet aggregation procedure. Potential platelet donors are matched against serum from platelet recipients to detect the presence of antibodies against donor platelets. If antibodies are present, it has been shown that these platelets would not be compatible and therefore have a shortened life span in the recipient. The question being asked is whether patients with no evidence of antibody by the above mentioned procedures would be able to survive normally or at least for an extended period of time in the recipient.

Manpower: E-3 (2 months)

Funding: $345.15 Consumable Supplies FY 1975

PROGRESS

Several patients have been evaluated, and patients with positive antibodies against platelets have now been obtained. Capability for performing platelet survival was established in the first week of April 1975, and the procedure will be set up in coordination with Nuclear Medicine to evaluate platelet survivals in patients in the near future.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of Specific and Total IgE Globulin Levels in the Serum to Specific Skin Tests

WORK UNIT NO.: C-18-74

PRINCIPAL INVESTIGATOR: Bryan R. Updegraff, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Robert Greely, M.D., Lieutenant Colonel, MC
Robert J. Lull, M.D., Lieutenant Colonel, MC
Charles Lewis, M.D., Lieutenant Colonel, MC

OBJECTIVES

To correlate the levels of specific circulating antibodies in the serum with intracutaneous skin tests in mountain cedar sensitive patients.

TECHNICAL APPROACH

A total of 50 patients will be selected from the Allergy Clinic for study. Ten will be placed in each of five groups based on reactivity of skin tests to mountain cedar antigen as graded from 0-4+. These patient's serum will be evaluated for levels of total and specific IgE and the results correlated.

Manpower: None

Funding: $ 999.00 Consumable Supplies FY 1974
$1,230.00 Consumable Supplies FY 1975

PROGRESS

Fifty patients were studied with skin tests and serum IgE (Fc specific to mountain cedar). Results were evaluated to show that a positive skin test correlated to a positive RAST but the correlation was not direct so that a more reactive skin test did not correlate to a more reactive RAST (serum Fc specific IgE).

C-18-74 (Continued)

In addition, 25 patients, who were treated with hyposensitization to Mountain Cedar, were studied before and at the end of the season and compared to the placebo treated group of 25 patients. The results show a significant reduction in RAST levels in treated group but no change in the untreated group.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy of Minocycline in Patients with Staphylococcal Skin Infections.

WORK UNIT NO.: C-19-74

PRINCIPAL INVESTIGATOR: Stephen E. Rostan, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Stuart Salasche, M.D., Major, MC
Barry L. Davison, M.S., Captain, MSC

OBJECTIVES

To demonstrate the clinical and laboratory efficacy of minocycline in patients with staphylococcal skin infections compared to phenoxymethyl penicillin.

TECHNICAL APPROACH

Thirty patients with suspected staphylococcal skin infections were treated for 7 days with either minocycline or phenoxymethyl penicillin in a double-blind fashion. Cultures were done on day 1, 3 and 7. Positive staphylococcal cultures were tested for sensitivity and resistance by the Kirby-Bauer method of zone inhabitation to minocycline, phenoxymethyl penicillin, tetracycline, oxacillin, cephalothin and erythromycin. Clinical observations were recorded on each visit.

Manpower: None

Funding: $256.00 Consumable Supplies FY 1974

PROGRESS

Seventeen patients had staphylococcal infections. Minocycline appears to be as efficient as phenoxymethyl penicillin in the treatment of staphylococcal skin infections.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hypertension with Polycystic Kidney Disease.

WORK UNIT NO.: C-20-74

PRINCIPAL INVESTIGATOR: Daniel A. Nash, Jr., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the volume status and the renin-angiotensin system in patients with polycystic kidneys and unexplained hypertension and to clarify the mechanism(s) of the hypertension frequently present in patients with polycystic kidneys.

TECHNICAL APPROACH

Patients presenting with polycystic kidney disease, minimal renal insufficiency, and significant hypertension are admitted to this study. The patient's renin activity is determined in the context of measured peripheral volume and aldosterone production. Studies are performed during volume expansion, contraction, and normal-volemic. Alternative explanations for hypertension are thoroughly excluded. The relative implication of volume versus renin in early polycystic disease hypertension is thus evaluated.

Manpower: None

Funding: None

PROGRESS

Seven patients have been evaluated. Only four have selective renal venous renin values. The results suggest an overwhelming volume component, and vigorous diuresis has controlled blood pressure where vasodilators had been unsuccessful. However, significant right and left renal renin production differences seen in two of four patients remain unexplained.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Radioactive Serotonin Release Assay and Lymphocyte Thymidine Uptake as a Means of Platelet Antibody Identification.

WORK UNIT NO.: C-22-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the relative specificities of these assays and to evaluate their clinical usefulness.

TECHNICAL APPROACH

Platelet antibodies are studied by the Serotinin Release Assay as described in Journal of Clinical Investigation, January 1975. These are compred with an assay described in the New England Journal previously using the Lymphocyte Thymidine Uptake as a means of identifying platelet antibodies.

Manpower: None

Funding: None

PROGRESS

This procedure has been done on two patients who have demonstrated platelet antibodies by the Serotonin release; however, they have not demonstrated an antibody by the lymphocyte thymidine uptake mechanism. Evaluation of this procedure has continued in a limited fashion and has suggested that it is not useful for identifying platelet antibodies as initially described in the literature.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in the Presence of Varied Platelet Antibodies.

WORK UNIT NO.: C-23-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the capability of platelet function when stressed by a variety of platelet antibodies.

TECHNICAL APPROACH

Bleeding time is evaluated when transfused platelets are given to a patient with known platelet antibodies. Once the platelet antibody has been identified in the serum of a patient, this serum is incubated with normal platelets and platelet function is determined by measuring platelet factor III and doing platelet aggregation studies.

Manpower: E-2 (2 months)
E-3 (4 months)

Funding: $196.00 Consumable Supplies FY 1974
$420.00 Capital Equipment FY 1974

PROGRESS

Ten patients have entered the study but evaluation is incomplete at this time. Thusfar, there are indications that the platelet isoantibodies when present in the serum will inhibit platelet function and, in fact, cause platelet aggregation and destruction.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Platelet Factor Four to Evaluate Hypercoagulable States.

WORK UNIT NO.: C-24-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To look at the plasma of patients who have a possible setting of hypercoagulability and to evaluate their plasma for platelet factor four activity.

TECHNICAL APPROACH

Platelet factor IV is material released by platelets when coagulation occurs. It is thought that the releast of this material may occur when intravascular thrombosis occurs. This, of course, is connected with hypercoagulable states where there is intravascular thrombosis coagulation occurring spontaneously. Patients admitted for thrombophlebitis, pulmonary embolus, or undergoing extensive surgery requiring continued periods of bedrest will be evaluated.

Manpower: None

Funding: None

PROGRESS

Several patients in Cardiology Service have been evaluated. Slight difficulty with the platelet factor IV assay was initially demonstrated but this has been corrected.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ophthalmologic Manifestation of Candida Infection and Hypersensitivity to Candida in Rabbits.

WORK UNIT NO.: C-26-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the natural history of candida infection in the eye.

TECHNICAL APPROACH

Twenty New Zealand white rabbits were utilized for the study. The grouping of the rabbis and experimental procedures were outlined in the original protocol. At the time all animals were sacrificed, the eyes were submitted for quantitative culture which determined on the basis of number of organisms per gram of tissue obtained from one of the two eyes. The second eye was submitted for histologic examination with specific biopsies of the retina and uvea.

Manpower: None

Funding: $106.25 Consumable Supplies FY 1974

PROGRESS

This project has been discontinued temporarily due to problems related to organism toxicity for the rabbits as well as the technical difficulty in securing animal cages for the rabbits.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Randomized Comparative Study of Tobramycin and Gentamicin in Acute Urinary Tract Infections.

WORK UNIT NO.: C-27-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate and compare the effectiveness of these two aminoglycoside antibiotics in the treatment of acute urinary tract infections in hospitalized patients where those infections are the result of susceptible organisms.

TECHNICAL APPROACH

A total of 30 patients were treated in random order with either Tobramycin or Gentamicin at a dose of 1 mg/kg q 8 hrs intramuscularly. Both groups were treated for an average of 6.5 days. Sixteen patients received Gentamicin and fourteen patients received Tobramycin. Laboratory studies and evaluation of the patient included complete blood count with platelet estimate; SMA-12 plus 6; urinalysis; urine culture and when indicated susceptibility testing. All examinations were performed within 24 hours prior to starting of antibiotic therapy and were repeated every 5th day of antibiotic therapy. In addition, they were repeated every 24 hours after stopping therapy. A follow-up specimen of urine was obtained 5 to 10 days following the course of treatment.

Manpower: None

Funding: $390.00 TDY FY 1975

PROGRESS

In this group of patients acute pyelonephritis was diagnosed in six, acute cystitis in eight of the patient group treated with Tobramycin. Four patients had acute pyelonephritis and 12 had

C-27-74 (Continued)

acute cystitis in the group treated with Gentamicin. Mean serum levels one hour after dose of Tobramycin was 3.9 micrograms/ml and 3.6 micrograms/ml after a similar dose of Gentamicin. Thw two groups had a similar mean age. Abnormal renal function developed during therapy in three patients receiving Gentamicin but in only one patient receiving Tobramycin. Suprainfection with a resistant Providencia stuartii strain occurred during Tobramycin therapy on one occasion. Recurrence due to a different strain occurred twice in the Tobramycin treated group within one week after therapy had been completed, but only in one patient treated with Gentamicin had recurrence. One of the Gentamicin treated patients developed skin rash and eosinophilia which disappeared with cessation of drug therapy. These data suggest that Tobramycin is as effective as Gentamicin in the treatment of acute urinary tract infection and may be less nephrotoxic at a similar dose schedule.

"A Randomized Comparative Study of Tobramycin and Gentamicin in Acute Urinary Tract Infections." Presented at the Fourteenth Interscience Conference on Antimicrobial Agents and Chemotherapy in San Francisco, California, 9-12 September 1974.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Factor VIII Activity/Antigen Ratio in von Willebrand's Disease. I. Epinephrine Effect. (Collaborative Study with Walter Reed)

WORK UNIT NO.: C-30-74

PRINCIPAL INVESTIGATOR: Frederick R. Rickles, Major, MC, WRAIR

ASSOCIATE INVESTIGATOR: Robert P. Bowman, Major, MC

OBJECTIVES

To study the effect of a stress on Factor VIII production and reactivity.

TECHNICAL APPROACH

Stimulate patients with epinephrine and measure Factor VIII antigen and coagulant activity as well as platelet factor activity by several methods. Plasma will be collected over a two day period.

Manpower: None

Funding: None

PROGRESS

Terminated due to the small amount of data obtained from Brooke Army Medical Center patients and the large number of patients available to Dr. Rickles at other Eastern medical centers.

Status. Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Antacid Therapy on Recurrences of Duodenal Ulcer.

WORK UNIT NO.: C-32-74

PRINCIPAL INVESTIGATOR: Richard W. Welch, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Armand Littman, M.D.

OBJECTIVES

To determine whether antacid treatment in duodenal ulcer patients during asymptomatic periods prevents recurrences of complications.

TECHNICAL APPROACH

Double blind prospective trial of antacid vs. placebo to assess recurrence rate in duodenal ulcer progress.

Manpower: None

Funding: None

PROGRESS

There has been a high dropout rate due to reassignment of active duty personnel and inability of some patients to regularly take medicine four times daily. At the present time it appears that eight of 23 subjects entered will complete the study protocol. There are approximately 50 additional patients incorporated in this study at Hines VA Hospital. There have been no complications from the medication.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phytohemagglutinin Stimulation of Sarcoid Lymphocytes.

WORK UNIT NO.: C-36-74

PRINCIPAL INVESTIGATOR: Hobert L. Pence, M.D., Major, MC

ASSOCIATE INVESTIGATORS: William W. Burgin, M.D., Lieutenant Colonel, MC
Robert L. Greely, M.D., Lieutenant Colonel, MC

OBJECTIVES

To study phytohemagglutinin (PHA) stimulation of lymphocytes from patients with sarcoid and to investigate possible suppression of lymphocyte response by plasma from sarcoid patients.

TECHNICAL APPROACH

Described in protocol. This involves studying blastogenesis of the lymphocytes of patients with sarcoidosis in presence of autologous or homologous AB + blood.

Manpower: E-6 (6 months)

Funding:

$2,068.50	Consumable Supplies	FY 1974
$ 475.00	Capital Equipment	FY 1974
$1,418.82	Consumable Supplies	FY 1975

PROGRESS

Seven patients have been studied with sarcoidosis. The plasma of six of the patients caused significant suppression of their lymphocyte responses to PHA. Because of the small number of patients found for the study, no correlations can yet be made concerning suppression of lymphocyte response by plasma and extent or severity of the disease. These preliminary results do look encouraging however.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Evaluation and Treatment of Male Infertility.

WORK UNIT NO.: C-39-74

PRINCIPAL INVESTIGATOR: Carlos E. Menendez, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., Colonel, MC
Mauro P. Gangai, M.D., Caolonel, MC

OBJECTIVES

To rule out any surgically or medically correctable causes of male infertility and to treat the idiopathic oligospermic or astheospermic infertile patient with human gonadotropin (Human chorionic gonadotropin).

TECHNICAL APPROACH

The male partners of infertile couples will be evaluated initially with a semen analysis. If this is abnormal in any way then they will be evaluated by an endocrinologist. If no specific endocrine syndrome is found, the patient will then be referred to Urology for a biopsy of the testes. This is done to differentiate the patient who has normal seminiferous tubule function with blockade of the exit tubes from those who have primary seminiferous tubule hypofunction. The patient who have no blockade of the tubes will then be given the opportunity to participate in this program which consists of injecting them with human chorionic gonadotropin once a week for a minimum of six months with periodic physical examinations and assays for testosterone and semen analysis. Patients who have a specific endocrine syndrome or a urological defect will receive the therapy indicated and will not be entered into the study.

Manpower: None

Funding: None

PROGRESS

Four men have entered this study and no conclusive results have been found, but we have noted other pathology as a result of our careful

C-39-74 (Continued)

examinations and these people have been treated accordingly. The men on the treatment are undergoing periodic semen analysis and testosterone assays and, although we think it will be beneficial, it is not efficacious in every case.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effectiveness of Immunotherapy in Mountain Cedar Pollinosis.

WORK UNIT NO.: C-43-74

PRINCIPAL INVESTIGATOR: Hobert L. Pence, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Bryan Updegraff, M.D., Major, MC

OBJECTIVES

To evaluate the role and effectiveness of allergy injection therapy with Mountain Cedar pollen extract in the treatment of hay fever and asthma caused by the pollen of this plant.

TECHNICAL APPROACH

Forty patients with proven Mountain Cedar pollinosis were divided into two groups of twenty each. One group was given immunotherapy with Mountain Cedar Extract during past pollen season and one group was given placebo. Patients were followed through the season in a double-blind controlled manner to quantitate symptoms and to evaluate effectiveness of immunotherapy.

Manpower: E 6 (6 months)

Funding: $172.74 Consumable Supplies FY 1975

PROGRESS

Thirty-two patients completed the study. Patients receiving immunotherapy had significantly fewer symptoms than those receiving placebo ($P < .01$). In addition, patients receiving immunotherapy had a drop in serum IgE against Mountain Cedar while those on placebo actually had a rise in specific IgE. This difference was significant ($P < .002$).

Presented to the Southwest Allergy Forum, Houston, Texas, 13 May 1975.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Early Diagnosis of Urinary Tract Infections.

WORK UNIT NO.: C-44-74

PRINCIPAL INVESTIGATOR: Leslie M. Burger, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate several methods of rapidly establishing the presence of significant bacteriuria.

TECHNICAL APPROACH

The accuracy of the urinalysis, nitrite test, and glucose test was compared with the urine culture in an effort to speed the diagnosis of urinary tract infections.

Manpower: None

Funding: $332.00 Consumable Supplies FY 1974
$ 27.16 Consumable Supplies FY 1975

PROGRESS

Thirty patients were studied. It became apparent that the incidence of false negative results was much greater than 50% with the glucose test and nearly as high with the nitrite test. The urine sediment - the number of bacteria seen and not the number of white cells - remains the most accurate if not the most expedient determinant.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Rejection of Verrucae Vulgaris - A Clinical Therapeutic Trial. Parts I and II. (Collaborative Study with Letterman)

WORK UNIT NO.. C-6-75

PRINCIPAL INVESTIGATOR: Joseph H. Greenberg, M.D., Major, MC (LAMC)

ASSOCIATE INVESTIGATORS: Charles W. Lewis, M.D., Lieutenant Colonel, MC
Nikolas Lapins, M.D., Major, MC

OBJECTIVES

To determine if induction of a delayed hypersensitivity reaction over a verruca vulgaris will cause destruction of the verruca and possibly cause regression of other verrucae vulgaris not treated.

TECHNICAL APPROACH

Patients with verrucae vulgaris agreeing to participate in the study have their warts treated either with topical Rhus oleoresin (if they have a positive history of Rhus dermatitis) or they receive an intradermal injection of one of the common skin test antigens into a wart. This group of patients is screened by testing with Mumps, Candida, PPD, SK-SD and Trichophyton, and the antigen giving the strongest reaction is selected for testing.

Manpower: None

Funding: None

PROGRESS

Sixty-two patients have completed the eight week follow-up period of the study. It appears that only SK-SD, Trichophyton and the Rhus antigen are effective in inducing a reaction in the warts significant enough to result in rejection of the wart virus.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Incidence of Transient Bacteremia During Bronchoscopy.

WORK UNIT NO.: C-8-75

PRINCIPAL INVESTIGATOR: Preston B. Cannady, Jr., M.D., Major, MC

ASSOCIATE INVESTIGATORS: Theodore R. McNitt, M.D., Major, MC
William W. Burgin, Jr., M.D., Lieutenant Colonel, MC
Robert B. Blumer, M.D., Lieutenant Colonel, MC

OBJECTIVES

To determine the incidence of bacteremia as a result of bronchoscopy using the fiberoptic bronchoscope.

TECHNICAL APPROACH

Patients undergoing diagnostic bronchoscopy, after having given informed consent, had throat cultures performed. Following throat cultures, a blood culture was obtained at time zero. Bronchoscopy was performed and at 5, 15 and 30 minutes following bronchoscopy, blood cultures were obtained for aerobic and anaerobic specimens. Bronchial washings were cultured during the bronchoscopy and these culture results compared.

Manpower: None

Funding: $4,705.00 MEDCASE FY 1975

PROGRESS

Twenty-five patients have been included in the study. The 25 patients did not include any patient who had been on antibiotics within three days of the study or who had either clinical or bacteriological evidence of sepsis or bronchopulmonary infections. Of the 25 patients, 11 had a single positive blood culture. The organisms isolated included Staphylococcus epidermidis in 4; Propionibacterium acnes in 5, Serratia Marcescens in 1 and Corynebacterium species in 1. Three additional patients had

C-8-75 (Continued)

two blood cultures positive for Staphylococcal Epidermidis. Throat cultures were unrewarding and bronchial washings were positive in 19 of the 25 patients. In only two patients were the organisms obtained by blood culture similar to those obtained by bronchial washings. Both of these organisms were Staphylococcus Epidermidis. No correlation existed between the length of the procedure, whether or not bursching or biopsy was performed and the presence of positive blood cultures. Clinical sepsis did not occur in any patient post bronchoscopy as evidenced by the absence of fever or hypotension.

This study supports evidence recently published concerning the absence of significant bacteremia during bronchoscopy. It was felt that the high incidence of positive cultures were related to technical aspects of blood culturing and represented skin contaminants. There is no evidence to support the use of S.B.E. prophylaxis in patients undergoing fiberoptic bronchoscopy, contrary to the present recommendations of the American Heart Association regarding stiff tube bronchoscopy.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Outpatient Algorithm Validation - A Pilot Study.

WORK UNIT NO.: C-9-75

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Leslie M. Burger, M.D., Lieutenant Colonel, MC
Richard K. Tompkins, M.D., Dartmouth Medical School

OBJECTIVES

To determine if clinical outpatient algorithms originally used to treat civilian outpatient populations can be validated and improved in a military outpatient environment - a Phase I study.

TECHNICAL APPROACH

Patients presenting to the BAMC AMIC with complaints of upper respiratory infection, cough, or ear problems were evaluated utilizing a Dartmouth/MEDEX standardized data collection sheet. Their laboratory evaluation and therapy were determined by a Dartmouth/MEDEX problem oriented Clinical Algorithm. Patients were then randomly selected to be blindly re-examined by a Board Certified Internist who ordered laboratory work and therapy as he felt indicated, based on his clinical judgment. Patients not randomized to be seen by the physician went home on the algorithm-directed therapy. Two weeks later, charts of both groups were examined and the patients contacted by phone. Based on the history, physical examination, laboratory results, and clinical course, patients were respectively placed in diagnostic categories and the results of this complete patient encounter entered into the Dartmouth/MEDEX computer system for analysis.

Manpower: None

Funding:			
	$3,125.00	Consumable Supplies	FY 1975
	$ 75.00	TDY	FY 1975

C-9-75 (Continued)

PROGRESS

Approximately 1300 patient encounters from the AMIC and an additional 250 duplicates certified by the internists have been entered into the computer for analysis. Preliminary examination of the data on patients evaluated using the URI algorithm shows no population differences between the two groups or between either of the two groups and a reference group of patients seen by physician extenders utilizing the same algorithm system at a private "fee for service" clinic in New Hampshire. In addition, this preliminar data indicates no difference in outcome between patients seen in the AMIC and patients seen by the internist except for the larger average laboratory costs of the patients seen by the internists.

A preliminary evaluation on the patients evaluated shows the need to examine a larger number of patients in order to include sufficient patients with ear complaints, and cough complaints, to make a statistical analysis of those two algorithms valid.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy of Topical Haloprogin in the Treatment of Chronic Tinea Pedis. A Phase II Study.

WORK UNIT NO.: C-13-75

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Frank L. Foreman, M.D., Major, MC

OBJECTIVES

To determine if 5% haloprogin cream is useful in the treatment of tinea pedis.

TECHNICAL APPROACH

This is a double blind efficacy study of 5% haloprogin cream and 1% haloprogin cream using patients of any race, over age 12 years, of either sex, who have chronic tinea pedis infection (greater than 3 months duration).

Manpower: None

Funding: None

PROGRESS

Twenty-one patients have been incorporated into the study. Data will be analyzed after fifteen additional patients are studied.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ibuprofen (Motrin^{R}) in the Treatment of Rheumatoid Arthritis.

WORK UNIT NO.: C-14-75

PRINCIPAL INVESTIGATOR: William J. Arnold, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effectiveness of a new nonsteroidal anti-inflammatory agent in patients with active rheumatoid arthritis over a 12-week period of observation.

TECHNICAL APPROACH

A maximum of 20 patients with "probable", "definite" or "classical" rheumatoid arthritis will be included in the study. Each patient will receive Ibuprofen 400 mg QID initially - dosage may vary from 400 to 2400 mg daily according to the individual's response. This regimen will continue for 12 weeks, and the patient will be seen 1, 2, 4, 6 and 12 weeks following entry into the study. Before receiving Ibuprofen and on each subsequent study visit, a history and physical exam will be performed.

Manpower: None

Funding: None

PROGRESS

Eight patients with classical, sero-positive rheumatoid arthritis participated in this project. Each patient was begun on 1600 mg of Motrin daily in divided doses and seen 1, 2, 4, 6, and 12 weeks after beginning the study. On each visit the patient was asked to gauge his or her arthritic process as to whether they felt poor, fair or good. Also objective joint exam on each visit was graded similarly. Each patient had at least a CBC at the beginning and end of the study.

C-14-75 (Continued)

The results of therapy with Motrin in these patients can be divided into two groupings: Treatment failures and Treatment successes.

1. Treatment Failures - 50% or 4 out of 8 patients.

a. Failure due to ineffectiveness of drug.

Patient M.M. had a full three month course of Motrin therapy to a maximum dose of 2400 mg per day with no subjective or objective improvement.

Patient J.E. refused to continue the study after one month on Motrin, 1600 mg daily, because of clinical deterioration after discontinuing Indocin prior to beginning Motrin.

b. Failure due to drug-related side effects.

Both of these patients experienced transient side effects which disappeared completely after discontinuing Motrin.

Patient A.B. was begun on Motrin, 1600 mg daily, in addition to 8 Ascriptin tablets daily. After 72 hours she developed nausea and vomiting and discontinued Motrin.

Patient M.G. experienced stabbing epigastric pain with nausea and vomiting and diarrhea after taking the third (400 mg) Motrin Tablet. She also discontinued the drug.

2. Treatment Successes - 50% or 4 out of 8 patients.

In this category not all patients improved to the same degree nor has that initial improvement been maintained. Moreover, each patient who did improve required the maximal dosage (2400 mg) of Motrin.

Patient E.H. improved both subjectively and objectively while on 2400 mg of Motrin daily. However, coincident with this improvement the RA Latex titer decreased from 1:5120 to 1:1280 and the Westergren ESR from 60 to 33 mm per hour. This lab improvement is not likely due to Motrin but suggests that she experienced coincidental natural remission of her disease during Motrin therapy.

Patient E.B. improved during the study period while on 1600 mg of Motrin daily but has since required 2400 mg daily for increased arthritis activity.

C-14-75 (Continued)

Patient K.C. noted subjective improvement while on 2400 mg daily but did not demonstrate objective improvement.

Patient R.L. received initial benefit from 1600 mg daily but subsequently has required 2400 mg to maintain improvement.

LABORATORY DATA: No significant alteration of hemoglobin, hematocrit, WBC count or differential WBC count was noted during the three month study period.

It is concluded from this obviously small study that Mortin is an effective anti-inflammatory agent in some, but not all patients with rheumatoid arthritis. Those side effects observed were transient and completely reversible with discontinuation of the drug. It is of note that those patients who did improve required the maximum allowable dosage of Motrin. Therefore, while Motrin will be a useful adjunct in the therapy of rheumatoid arthritis, it should be employed only after the patient has not improved on an adequate regimen of salicylates, bedrest and physical therapy, and with a realization of the potential expense and variable effectiveness in an individual patient.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in Patients Undergoing Therapy with Velban and Bleomycin.

WORK UNIT NO.: C-17-75

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate patients undergoing intensive chemotherapy with Velban and Bleomycin for determination of platelet function abnormalities induced by these agents.

TECHNICAL APPROACH

Patients receiving chemotherapy with these agents are being studied by platelet function studies to include bleeding time and platelet aggregation.

Manpower: None

Funding: None

PROGRESS

Several patients have been studied and initial indication is that there is no platelet function abnormality with those agents.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in Patients Undergoing Vincristine Therapy.

WORK UNIT NO.: C-18-75

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine any abnormalities of platelet function occurring in patients who are treated with Vincristine therapy.

TECHNICAL APPROACH

Patients obtaining Vincristine as a single agent or as a single agent prior to other chemotherapy, are evaluated with platelet function studies to include bleeding time and aggregation, clot retraction and PTT being performed. The evaluation of changes due to a chemotherapeutic agent is noted.

Manpower: None

Funding: None

PROGRESS

Three patients have been studied to date. Thusfar, no indication of a functional abnormality has been demonstrated in patients receiving Vincristine therapy.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Renal Handling of Bicarbonate in Patients with Hyperparathyroidism.

WORK UNIT NO.: C-22-75

PRINCIPAL INVESTIGATOR: David B. Olin, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the effect of parathyroid hormone on bicarbonate absorption in the human model.

TECHNICAL APPROACH

Patients with clinically suspected hyperparathyroidism will be asked to undergo sodium bicarbonate infusion to check tubular reabsorption of bicarbonate over range of serum bicarbonate. Glomerular filtration rate will be calculated using inulin clearance. After the patient has exploratory procedure for adenoma, a postoperative study will be performed to see if a difference can be shown before and after parathyroidectomy.

Manpower: None

Funding: None

PROGRESS

No patients have been entered into the study.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Isolation of Deoxyribonucleic Acid (DNA) and Anti-DNA Complexes.

WORK UNIT NO.: C-24-75

PRINCIPAL INVESTIGATOR: Roy S. Adaniya, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To isolate circulating DNA-anti DNA complexes in patients with systemic lupus erythematosus (SLE) utilizing Agarose 4B gel filtration.

TECHNICAL APPROACH

Utilizing the solid phase radioimmunoassay method of Kredich, sera from patients were tested for antibody against native double strand DNA. Those specimens given positive assay were studied.

Positive sera were fractionated in Agarose 4B to separate the larger DNA and DNA immune complexes from gamma globulins. Each gamma globulin fraction was tested for antibody against DNA.

Manpower: None

Funding: None

PROGRESS

Patients that were positive for antibodies against DNA were identified. The first portion of the investigation was directed towards the determination of what specific mixes of scintillation fluid and quantity of labeled DNA would yield the most efficient solubilization of aqueous solutions and recovery of maximal disintegrations per minute. It was determined that use of 0.5 cc aliquots of fractions added to combination of Bray's solution with 0.5 cc methanol added gave the most efficient results.

C-24-75 (Continued)

The Agarose column was poured. The void volume was determined to be at 120 cc, with a Ve/Vo of 2.7 for IGG. Utilizing several patients, the ratio Ve/Vo was a constant at 2.7-2.8.

Taking 0.5 cc aliquots from various fractions, the fractions were tested for the presence of antibodies against DNA. In the Ve/Vo ratio of 1.7, specific antibody against a DNA was discovered. This is the ratio at which IgM is eluded from the fraction. Although molecular weight determinations have not been performed, this is a fraction where rheumatoid factor has been eluted by Dr. Persellin's laboratory.

Status: Terminated due to transfer of principal investigator

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Incidence and Characterization of Adrenal Insufficiency in Oat Cell Carcinoma.

WORK UNIT NO.: C-25-75

PRINCIPAL INVESTIGATOR: K. James Ehlen, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Roger L. Wallace, M.D., Captain, MC
Steven Humphrey, M.D., Captain, MC
Carlos E. Menendez, M.D., Major, MC
Hayden Braine, M.D., Major, MC

OBJECTIVES

To establish the incidence and character of adrenal insufficiency in patients with oat cell carcinoma.

TECHNICAL APPROACH

Evidence of adrenal insufficiency is sought systematically in patients with oat cell carcinoma by utilizing two different modes of testing.

1. ACTH stimulation - 4 hours with serum cortisol measured before and after.
2. Metapyrone test with pre and post measurements of serum cortisol, serum 11-Desoxycortisol (CPD S) and plasma ACTH.

Manpower: None

Funding: $1292.00 Consumable Supplies FY 1975

PROGRESS

Twelve patients have been tested. Results show no evidence of adrenal insufficiency in any patient. Repeat testing at six month intervals is anticipated.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Basal Blood Pressures and Casual Blood Pressures Effecting the Therapy of Hypertension.

WORK UNIT NO.: C-26-75

PRINCIPAL INVESTIGATOR: Marvin Goldberg, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Richard Merrill, M.D., Major, MC

OBJECTIVES

To determine if basal blood pressure taken three times daily by the patient or another trained person is significantly different than the casual blood pressure taken during clinic visits.

TECHNICAL APPROACH

Patients are taught to take blood pressures three times daily at home. They record this data and show it only to the physician conducting the study. The clinic physicians, who are adjusting the patient's medication according to the blood pressure at the time of the clinic visit, are not aware of the patient's daily blood pressures taken at home.

Manpower: None

Funding: None

PROGRESS

Six patients have entered study.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: In Vitro Lymphocyte Stimulation and Leukocyte Inhibitory Factor Assay in Patients Who Have Been Immunized Against Rabies.

WORK UNIT NO.: C-27-75

PRINCIPAL INVESTIGATOR: Adolf E. Rahm, Jr., M.D.
Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study in vitro lymphocyte stimulation and leukocyte migration inhibition in patients who have been immunized against rabies.

TECHNICAL APPROACH

Blood is drawn from patients who have been immunized against rabies with duck embryo vaccine. Two in vitro analyses are run, one in which lymphocytes are separated from the patient's blood and stimulated in vitro with vaccine to see if blastogenesis occurs. This technique is used to demonstrate lymphocyte activity in rabies immunity. The second technique is Leukocyte Inhibitory Factor Assay in which the patient's leukocytes are incubated in the presence of an antigen (rabies vaccine). In patients who have developed lymphocytic immunity to a given antigen, migration of leukocytes is inhibited.

Manpower: None

Funding: None

PROGRESS

Initially lymphocyte stimulation was studied using duck embryo vaccine. In nine controls and fourteen subjects, it was determined that duck embryo vaccine contains a nonspecific stimulator since

C-27-75 (Continued)

both controls and rabies immunized subjects demonstrated lymphocyte blastogenesis. Another vaccine which is grown in suckling mouse brain tissue was then tried. Five controls and ten subjects have been studied. This vaccine appears to be successful since individuals who have been immunized against rabies demonstrate lymphocyte blastogenesis and those who have not been immunized do not demonstrate lymphocyte blastogenesis. In addition, leukocyte migration inhibition occurs in patients who have been immunized against rabies and does not occur in controls when lymphocytes and other leukocytes are incubated in vitro in the presence of mouse tissue vaccine.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Measurement of Transepidermal Water Loss in Anhidrotic Ectodermal Dysplasia and Erythroderma.

WORK UNIT NO.: C-29-75

PRINCIPAL INVESTIGATOR: Robert L. Rietschel, M.D., Captain, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To measure total body evaporative water loss in skin conditions of excessive and insufficient transepidermal water loss and compare these values with measurements of water loss from small areas of skin.

To study the effect of various topical compounds in common dermatologic use on transepidermal water loss in individuals with excess or insufficient water loss.

TECHNICAL APPROACH

The Meeco electrolytic water analyzer will be used to measure transepidermal water loss in individuals with abnormal water loss as outlined in the investigational protocol. The ability of topical compounds to alter the transepidermal water loss will be studied with this instrumentation.

Manpower: None

Funding:	$ 255.95	Consumable Supplies	FY 1975
	$1,250.00	MEDCASE	FY 1975

PROGRESS

Equipment has been ordered, but not received.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Role of the Prostaglandins (PG) in the Response to Volume Expansion in the Dog. (Collaborative Study with Institute of Surgical Research)

WORK UNIT NO.: C-30-75

PRINCIPAL INVESTIGATOR. David B. Olin, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Richard H. Merrill, M.D., Major, MC
Marvin Goldberg, M.D., Major, MC

OBJECTIVES

To evaluate in the dog model of volume expansion, the role of prostaglandins and to determine if the prostaglandins play a role in renal autoregulation.

TECHNICAL APPROACH

Mongrel dogs of varied sex will be studied at the USAISR Laboratory. Studies will be performed on hydropenic dogs anesthetized with pentobarbitol and respirations supported in Bird respirator. After control periods, data for GFR, renal blood flow, Cosm, $U_{Na}V$, the animals will be volume expanded with Ringers lactate at 10% of estimated blood volume over 30 minutes. VE will be maintained with replacement of urine output and after 30-60 minutes, the animals will be treated with 2 mg/kg IV Indomethacin or Meclofenamate with further observations of GFR, RBF, $U_{Na}V$, Cosm, etc. A similar group of dogs will be treated with Indomethacin or Meclofenamate prior to VE.

Manpower: None

Funding: None

PROGRESS

Initial work has just begun at the USAISR and only one dog has been studied at this time.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: To Determine Whether the Prostaglandins are Important in the Development of Acute Renal Failure. (Collaborative Study with USA Institute of Surgical Research)

WORK UNIT NO.: C-31-75

PRINCIPAL INVESTIGATOR: David B. Olin, M.D., Major, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To investigate possible pathophysiologic mechanisms in gentamicin acute renal failure.

TECHNICAL APPROACH

New Zealand white rabbits, 2-4 kilogram in size with random sex, will be utilized. Initially two groups will be injected with 40 mg/kg and 80 mg/kg dosage to see if any effect can be found. After two weeks of daily injection, the animals will be sacrificed and tissues examined by light electron microscopy, and scanning electron microscopy.

Three groups will be created - 1) Volume depletion - diuretic therapy; 2) Acidosis by ammonium chloride diet supplement; and 3) Prostaglandin inhibition by treatment with Indomethacin.

Manpower: None

Funding: None

PROGRESS

Initial work with two groups receiving 40 mg/kg and 80 mg/kg Gentamicin has been completed. Subsequent groups will be started in the next month.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Simple Biochemical Test for the Screening of Malignancies.

WORK UNIT NO.: C-33-75

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Harris D. Plant, SP3

OBJECTIVES

To examine the reaction of Ehrlich's reagent with human plasma and to determine if the intensity of the reaction can be correlated with the health of that individual.

TECHNICAL APPROACH

Plasma from at least 50 patients in each of four groups will be examined. Group I will consist of patients diagnosed as having an uncontrollable malignancy; Group II - Patients who have had successful anti-cancer treatment; Group III - Patients with nonmalignant diseases; and Group IV - Control group.

One 7 ml EDTA tube will be collected from each patient, centrifuged, and the plasma removed. Plasma will be frozen following preparation and thawed immediately prior to use. 2 cc of plasma, 4 cc distilled water, and 1 cc of Ehrlich's reagent are mixed in a test tube, incubated 7 hours at 56°C, centrifuged 15 min at 2000 rpm and the optical density of the supernatant read at 640 nm on the ACTA spectrophotometer. Variances of the four test groups will be analyzed for statistical significance by students paired t-test using an Olivetti P602 computer.

Manpower: None

Funding: None

PROGRESS

This is a new study and no patients have been entered into the protocol to date.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Sperm Antibodies in Vasectomized Men.

WORK UNIT NO.: C-3-72

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the onset of sperm antibody production postvasectomy with special attention to serum uric acid values prior to and after vasectomy.

TECHNICAL APPROACH

Blood was obtained prior to, 6 weeks, 6 months, 12 months, 24 months, and 36 months following bilateral vas ligation. The serum was removed after centrifugation of the clotted blood, and complement was destroyed by applying heat at 56° Celsius for 30 minutes.

The macroscopic gelatin sperm-agglutination test of Kibrick et al. and the sperm-immobilization test of Isojima et al. were used to determine the presence of sperm antibody activity in the sera. Pooled untreated rabbit sera served as the complement source. Fresh semen obtained from sperm donors, whose counts were consistently above 60 million spermatozoa per milliliter coupled with motility greater than 70%, was used as the antigen.

Uric acids were determined on the pre- and postvasectomy sera by the manual method as adapted by Technicon.

Manpower: None

Funding: None

C-3-72 (Continued)

PROGRESS

Thirteen men have been followed through 36 months postvasectomy. None had sperm-agglutinating or sperm-immobilizing activity prevasectomy, two remained negative at each study interval, eight became negative by 36 months, and three remained positive for sperm-agglutinating activity with titers 1:16, 1:64, and 1:128 (two of the latter also showed sperm-immobilizing antibodies at titers 1:16 and 1:32).

Serum uric acid levels on these 13 men pre-, 6 weeks, 6 months, 12 months, 24 months, and 36 months postvasectomy showed no statistical increases (t-tests) but there was a significant transient decrease at 12 months when compared to prevasectomy uric acid levels.

Status: Completed

Presented at the 22nd Annual James C. Kimbrough Urological Seminar, 13 November 1974, San Antonio, Texas.

Presented at N.I.H. Contractors Workshop on Vasectomy, 19 February 1975, Asilomar, Pacific Grove, California.

Presented at Luncheon Conference, 31st Annual Meeting of the American Fertility Society, 3 April 1975, Los Angeles, California.

Published as part of Vas Ligation: Sperm Antibodies, in Control of Male Fertility, edited by J. J. Sciarra, C. Markland, and J. J. Speidel. Harper & Row, Hagerstow, Maryland, 1975, pp 189-195.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Heart Valve Prosthesis in Pregnancy - Review of the Literature and Report of Three Cases.

WORK UNIT NO.: C-36-72

PRINCIPAL INVESTIGATOR: Warren N. Otterson, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To analyze the effect of heart valve prostheses on maternal morbidity and mortality, perinatal mortality, and general reproductive performance. In addition, it is hoped that a sound program of management, especially regarding the use of anticoagulant drugs, will evolve as a result of an extensive review.

TECHNICAL APPROACH

The world literature and Brooke Army Medical Center case reports were reviewed and analyzed relative to maternal and fetal outcome. The role of anticoagulants in patient management was evaluated.

Manpower: None

Funding: None

PROGRESS

Females in the reproductive years with heart valve prostheses should postpone pregnancy for 2 or 3 years following insertion. Cardiac function should be thoroughly evaluated prior to pregnancy. Anticoagulation is indicated throughout. Heparin would theoretically be advisable, but probably not mandatory during the first 12 weeks, followed by oral anticoagulants until approximately 34-36 weeks, then reinstituting heparin through labor and delivery.

C-36-72 (Continued)

Patients with mitral valve prosthesis should receive special attention as to cardiac hemodynamic evaluation, close control of anticoagulation, and close observation for congestive heart failure and valve malfunction. Antibiotics should be given routinely in labor and for at least 2-3 days postpartum.

Status: Completed

Presented at the 23rd Armed Forces Seminar on Ob-Gyn, 3-8 November 1974, Washington, D.C.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Use of Oxytocin Challenge Test in Monitoring High Risk Pregnancies.

WORK UNIT NO.: C-31-74

PRINCIPAL INVESTIGATOR: Bernard L. Hayden, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Joe Leigh Simpson, M.D., Major, MC

OBJECTIVES

To determine (1) if the oxytocin challenge test (OCT) alone can successfully predict the outcome of high risk pregnancies and (2) if the presence of meconium in utero signifies fetal distress.

TECHNICAL APPROACH

During an 8 month interval, 105 patients were considered to have a high probability for developing placental insufficiency. Prior to inclusion in this investigation, each patient was assessed by two or more independent observers. In every instance, the fetal biparietal diameter was determined by ultrasound at 20 weeks gestation or when the patient was diagnosed initially. Abnormal ultrasound determinations were repeated every 2-3 weeks. The results of certain other parameters utilized in monitoring high risk pregnancies were correlated with the results of the OCT. The following patients were evaluated: Patients with diabetes mellitus; post-date fetuses; chronic hypertension; pre-eclampsia; suspected IUGR; elderly primagravidas; and history of unexplained stillborn.

Manpower: None

Funding: None

PROGRESS

Among 105 patients with an increased risk of placental insufficiency, no fetal deaths occurred. There were no intrauterine deaths in this group of high risk pregnancies.

C-31-74 (Continued)

Conclusions: The OCT can serve as the primary method for assessing intrauterine status of the fetus with suspected placental insufficiency. Fetuses with a positive OCT and an L/S ratio of 2:1 should be delivered by cesarean section. Fetuses with a suspicious OCT should be restudied within 72 hours. Patients with a negative OCT can be allowed to terminate their pregnancies spontaneously, albeit with monitoring during labor.

Status: Completed

Presented at the 23rd Annual Armed Forces Seminar on Obstetrics and Gynecology, Washington, D.C. 3-8 November 1974.

Hayden, B.L., Simpson, J.L, Ewing, D.E., and Otterson, W.N.: Can the Oxytocin Challenge Test serve as the primary method of monitoring high risk pregnancies? Accepted for publication in Obstetrics and Gynecology.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cefazolin as a Prophylactic Antibiotic in Vaginal Hysterectomy.

WORK UNIT NO.: C-37-74

PRINCIPAL INVESTIGATOR: Willie J. Lett, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Barry L. Davison, M.S., Captain, MSC
Rudi Ansbacher, M.D., Colonel, MC
Warren N. Otterson, M.D., Colonel, MC

OBJECTIVES

To compare the effectiveness of one dose of cefazolin to three doses of cephaloridine as a prophylactic antibiotic in vaginal hysterectomy.

TECHNICAL APPROACH

Patients undergoing vaginal hysterectomy from March 1974 to February 1974 were placed in a group receiving cefazolin, cephaloridine, or no medication. One hour prior to operation each received IM cefazolin or cephaloridine. Those on cephaloridine received 1 gm immediately and 12 hours postoperatively. 1 gm of vaginal cuff was taken intra-operatively for aerobic and anaerobic cultures. Four blood cultures for anaerobic and aerobic organisms were drawn in equally spaced time periods for 24 hours in patients with febrile postoperative course. Febrile morbidity was defined as temperature elevation greater than 100°F after the first 24 hours post-op on two occasions, 6 hours apart. Febrile patients had vaginal cuff cultures done on the day of diagnosis for aerobic and anaerobic organisms.

Manpower: None

Funding:			
	$1,064.99	Consumable Supplies	FY 1974
	$2,433.46	MEDCASE	FY 1975
	$ 150.00	Consumable Supplies	FY 1975

PROGRESS

Data have been collected and are now being analyzed.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Laminaria: Two Outpatient Uses.

WORK UNIT NO.: C-38-74

PRINCIPAL INVESTIGATOR: Jose R. Ossorio, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., Colonel, MC
Warren N. Otterson, M.D., Colonel, MC

OBJECTIVES

To determine if by the use of laminaria tents, sufficient dilatation of the cervix can be obtained in patients with stenotic or tight cervical ossa, so as to enable easier endometrial sampling by endometrial biopsy or jet washing, and easier insertion of intrauterine devices in nulliparous patients.

TECHNICAL APPROACH

One hundred patients seen in the outpatient Gyn Clinic who are found to have tight cervical ossa which do not permit sounding with a regular uterine sound but who tolerate the introduction of a wire sound will have a size thin or extra thin laminaria tent inserted. The removal of the laminaria tent and the subsequent intrauterine instrumentation either for endometrial sampling or intrauterine device insertion will be accomplished 3-4 hours later as an outpatient procedure. The technique of insertion to be used will be similar to the one recommended by Hale and Pion.

Manpower: None

Funding: $330.00 Consumable Supplies FY 1974

PROGRESS

Thirty-two patients have entered the study. No failures or complications have occurred.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Testicular Biopsy: Sperm Antibodies.

WORK UNIT NO.: C-10-75

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Mauro P. Gangai, M.D., Colonel, MC

OBJECTIVES

To determine whether sperm-agglutinating and sperm-immobilizing antibodies can be detected in the sera of men after testicular biopsy.

TECHNICAL APPROACH

Ten milliliters of blood were obtained from nine men with oligospermia or azoospermia prior to and at 3, 7, and 14 days following testicular biopsies. The sera were removed after centrifugation of the clotted blood and complement was destroyed by applying heat of 56° Celsius for 30 minutes. They were stored at -25° Celsius until tested.

The macroscopic gelatin sperm-agglutination test of Kibrick et al. and the sperm-immobilization test of Isojima et al. were utilized to determine the presence of sperm antibody activity in the sera. Pooled untreated rabbit sera served as the complement source. Fresh semen, obtained from donors whose counts were consistently above 60 million spermatozoa per milliliter coupled with motility greater than 70%, was used as the antigen.

Two to four semen analyses were performed on each man prior to surgery.

Testicular biopsies were obtained by the open method in the operating room.

Manpower: None

Funding: None

C-10-75 (Continued)

PROGRESS

The men ranged in age from 20-34 years. One had sperm counts consistently greater than 30 million per milliliter, four had oligospermia, and four azoospermia on repeated semen analyses. None had sperm-agglutinating or sperm-immobilizing antibodies demonstrable in their sera either before or up to 14 days after testicular biopsies.

The biopsies revealed maturation arrest at various stages of spermatogenesis in six men, and three had germ cells present in all stages including mature spermatozoa but in decreased amounts.

Status: Completed

Presented at the 31st annual meeting of the American Fertility Society, Los Angeles, California, 3-5 April 1975.

Ansbacher, R. and Gangai, M.P.: Testicular biopsy: sperm antibodies. Accepted for publication in Fertility and Sterility.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Relationships of Vaginal and Cervical Flora in Pregnancy and Premature Rupture of Membranes.

WORK UNIT NO.: C-11-75

PRINCIPAL INVESTIGATOR: James E. Connerth, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Willie J. Lett, M.D., Major, MC
Barry L. Davison, M.D., Captain, MSC
Rudi Ansbacher, M.D., Colonel, MC
Warren N. Otterson, M.D., Colonel, MC

OBJECTIVES

To assess the possible degree of correlation between vaginal and cervical flora in pregnancy and premature rupture of membranes.

TECHNICAL APPROACH

Vaginal and cervical cultures are obtained on all new OB patients at the first visit, utilizing Anaswabs. The cultures are repeated in the third trimester of gestation. Amniotic fluid will be cultured in a group of control patients and those with premature rupture of membranes.

Manpower: None

Funding: $4,099.81 Consumable Supplies FY 1975

PROGRESS

One hundred and sixy patients cultured so far (all new OB patients) have shown good agreement between vaginal and cervical flora. Many anaerobic organisms are being identified (10 bacteroides CDC F_1) and several β-hemolytic streptococci.

We plan to correlate microflora between first and third trimester cultures with normal controls and those with premature rupture of membranes or postpartum morbidity.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of Phenotypic Sex of Fetuses with Amniotic Fluid Testosterone Levels.

WORK UNIT NO.: C-20-75

PRINCIPAL INVESTIGATOR: William Sutherland, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., Colonel, MC
Joe Leigh Simpson, M.D., Major, MC
Edward D. Helton, Ph.D., Captain, MSC
Harris D. Plant, SP3

OBJECTIVES

To determine whether testosterone levels in male fetuses, 16-20 weeks embryonic age, are significantly higher than those of female fetuses; and to determine whether the observed ranges of testosterone values will allow one to deduce phenotypic sex from the value of amniotic fluid testosterone.

TECHNICAL APPROACH

Fifty patients undergoing elective second trimester abortions at Brooke Army Medical Center over a six month period will be surveyed. Amniotic fluid will be obtained at the time an appropriate abortifacient is injected into the amniotic cavity. Assay for testosterone will be performed utilizing a method which incorporates procedural details set forth by Armando de la Pena (laboratory method), Burton V. Caldwell (laboratory notes on radioimmunoassay of steroids) and Hillier, Brownsey and Cameron with only slight modification by Helton and Plant for use with liquor amnii. Following abortion, fetal sex will be determined anatomically by at least two physicians, including one of the investigators. Ideally, one might determine the chromosomal complement of every aborted fetus, but this is not economically feasible. Discrepancies between phenotypic and genetic sex occur so rarely that statistical correlations are unlikely to be invalidated. Fetuses in which maceration precludes anatomical sex determination will be excluded from this investigation.

Manpower: Captain (3 months)
E-3 (4 months)

Funding: $436.79 Consumable Supplies FY 1975

C-20-75 (Continued)

PROGRESS

The radioimmunoassay has been established in the Clinical Investigation Laboratory and purification of the testosterone in the amniotic fluid sample is under way. Difficulties with the pigments present in the fluid have prevented accurate estimates of the androgens present but methods are being utilized to remove the pigments and allow accurate quantitative analysis by RIA.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Microbiologic Comparison of Therapeutic and Disc Antibody Activity Against Selected Enteric Bacteria.

WORK UNIT NO.: C-16-75

PRINCIPAL INVESTIGATOR: Mrs. Cleste N. Guerra, M.S.

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the sensitivity patterns of therapeutic antibiotics and antibiotic-impregnated discs.

To develop and perform antibiotic sensitivity tests designed to compare the effectiveness of both laboratory methods in relation to proper patient care.

To provide better laboratory indices by which physicians may more accurately assess the drug of choice in treatment of patient infections.

TECHNICAL APPROACH

Tube dilution tests of therapeutic and diagnostic (disc) Gentamicin were performed in conjunction with commercially-prepared Gentamicin disc tests against selected patient strains of Serratia sp. Known concentrations of therapeutic Gentamicin were performed in the order of 20, 10, 5.0, 2.5, 1.2, and .6 mcg/ml. The diagnostic disc 10 mcg (aqueous solutions) were diluted accordingly: 1:2, 1:4, 1:8, 1:16, 1:32 and 1:64. A total of 204 dilution tests were performed to compare with 17 disc sensitivities.

Manpower: None

Funding: None

PROGRESS

Preliminary results indicate that all strains tested were resistant except in four cases. However, it was noted that in these four the MIC (minimum inhibition concentration) was still higher than most

C-16-75 (Continued)

achievable blood levels. A comparison was made of all tests; i.e., therapeutic vs. diagnostic, tube sensitivities vs. disc sensitivities. A correlation of results was noted in these same four cases whereas all others were at variance with the routine disc sensitivity. It should be emphasized that this comparison was made between known dilutions of Gentamicin and inoculum and relatively unknown Gentamicin concentrations, size of inoculum, humidity, capillary action for absorption of the drug into the media and possible deterioration of disc strength. On the tube dilution study, control tests were performed and results were positive.

A presumptive evaluation of current results provide reasonable evidence that the disc sensitivity reported to clinicians, for guidance in patient treatment, is not necessarily consistent with actual conditions experimentally designed to test this theory.

The consistent patterns of this pilot study justify recommending the continuance of similar experiments with other selected antibiotics and bacterial strains to further examine the validity of the disc sensitivity test.

Status: Ongoing

Presented at the American Society for Microbiology, Texas Branch, meeting in Galveston, Texas, 25 October 1974.

Guerra, C.N.: A new approach: a taxonomic theory based on negative biochemical test reactions for identification of bacteria. Submitted to Applied Microbiology for publication.

Guerra, C.N.: Observations on the rapidity of biochemical reactions of a selected representative group of enteric bacteria. Submitted for publication in Applied Microbiology.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Investigation of Response of Lymphocytes to PHA as Affected by Prolonged Rupture of Membranes.

WORK UNIT NO.: C-37-73

PRINCIPAL INVESTIGATOR: Melvin Baden, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: M. Douglas Jones, Jr., M.D.

OBJECTIVES

To investigate the effect of labor and prolonged premature rupture of the membranes (24 hours) on radioactive thymidine incorporation by lymphocytes of newborn infants in response to phytohemagglutinins.

TECHNICAL APPROACH

The initial phse of this study will evaluate ten infants electively delivered by caesarean section to be used as controls. Ten infants born by vaginal delivery to primiparous women with less than 24 hours rupture of membranes and 10 infants with prolonged premature rupture of membranes greater than 24 hours will be investigated. Blood will be obtained from the fetal side of the placenta. The incorporation of radiothymidine in response to PHA will be measured in a scintillation counter after preparation of the lymphocytes by techniques already developed in this laboratory.

Manpower: None

Funding: $88.80 Consumable Supplies FY 1974

PROGRESS

This study is terminated due to inability of the associate investigator to complete evaluation of data acquired.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Cellular Immunity to the Varicella-Zoster Virus Employing a Newly Developed Microassay Technique.

WORK UNIT NO.: C-14-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Luis Canales, M.D., Colonel, MC
Monroe A. Vincent, B.S.
Sally A. Hensen, B.S.

OBJECTIVES

To examine the applicability of a newly developed microassay technique, which measures cellular immunity, specific to the Varicella-Zoster virus.

TECHNICAL APPROACH

In vitro assay of blastogenesis: lymphocytes are separated from whole blood and incubated with tissue culture cells persistently infected with the virus under investigation. Viruses have included Varicella-Zoster or other herpes group viruses. Uninfected cells were used as controls for the blastogenic index (BI) calculated from cpm of C-14 or ^{3}H thymidine uptake for lymphocytes incubated with infected cells divided by uptake following incubation with uninfected cells. This assay is being applied to study varied illnesses caused by herpes group viruses.

Manpower: None

Funding:

$ 165.20	Consumable Supplies	FY 1974
$1,112.50	Consumable Supplies	FY 1975
$ 695.00	Capital Equipment	FY 1975
$ 134.65	Reprints	FY 1975
$ 397.00	TDY	FY 1975

PROGRESS

Many viral infected cell lines have been examined for their efficacy and reproducibility in the blastogenic assay. Appropriate lots of

C-14-74 (Continued)

viral infected cell lines have been control rate frozen for storage in our vapor nitrogen tank. Lymphocyte to tissue culture cell ratios have been determined for the assays as well as kinetic studies. The assay has now been applied in the clinical setting in examining patients with severe viral infection, recurrent viral infection, and in studying patient on immunosuppressive therapy.

Status: Ongoing

Presented at the American Academy of Pediatrics meeting, San Francisco, California, 19-22 October 1974.

Steele, R.W., Chapa, I.A., Vincent, M.M., Hensen, S.A., Keeney, R.E.: Effects of adenine arabinoside on cellular immune mechanisms in humans. Antimicrobial Agents and Chemotherapy, 7:203-207, 1975.

Steele, R.W., Chapa, I.A., Vincent, M.M., Hensen, S.A., Keeney, R.E., Canales, L.: Adenine arabinoside: an anti-viral agent. Edited by D. Pavan-Langston, Robert A. Buchanan and Charles A. Alford, Jr. Raven Press, New York 1975.

Steele, R.W., Vincent, M.M., Hensen, S.A., Fucillo, D.A., Chapa, I.A., Canales, L.: Cellular immune response to Herpes-Simplex Virus I (HSV-1) in recurrent herpes labialis. In vitro blastogenesis and cytotoxicity to HSV-1 infected cell lines. J. Infect. Dis. 131, May 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cellular Immunity to Herpesvirus Hominis in the Compromised Host.

WORK UNIT NO.: C-15-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D., Major, MC
Luis Canales, M.D., Colonel, MC

OBJECTIVES

To develop specific and reliable in vitro assays of both the afferent and efferent mechanisms of cellular immunity to Herpes virus hominis (HVH) and to examine responses of patients with malignant disease or patients on immunosuppressive therapy.

TECHNICAL APPROACH

Utilizing tissue culture cells persistently infected with Herpes-Simplex 1 viruses as target cells, release of 51 Cr from these cells or controls is used as the index lymphocyte activity.

This cytotoxicity assay is being applied to study the immune responses of patients with varied illnesses caused by herpes group viruses.

Manpower: None

Funding:

$1,206.78	Consumable Supplies	FY 1974
$ 492,99	TDY	FY 1974
$ 504.00	Consumable Supplies	FY 1975

PROGRESS

Technical details of the cytotoxicity assay including the lymphocyte to target cell ratios and kinetics have been perfected so that the assay has been demonstrated to be sensitive, reliable and reproducible. Investigation has been expanded to include cell lines infected with the following viruses: Herpes-Simplex Virus Type I, Herpes-Simplex Virus Type II, Varicella Zoster Virus, Measles (Rubeola), Rubella, and Cytomegalo virus. Clinical situations examined to date included oncology

C-15-74 (Continued)

patients with Varicella Zoster infection, chronic viral infection, recurrent viral infection, subacute sclerosing panencephalitis, and patients treated with anti-viral agents.

"Specific Inhibitory Factors of Cellular Immunity in Children with Subacute Sclerosing Panencephalitis" presented at the American Academy of Pediatrics meeting San Francisco, California, 17 October 1974.

Steele, R.W., Hensen, S.A., Vincent, M.M., Fucillo, D.A., Bellanti, J.A.: Development of specific cellular and humoral immune responses in children immunized with live rubella virus vaccine. J. Infect. Dis. 130:44-453, Nov 1974.

Steele, R.W., Fucillo, D.A., Hensen, S.A., Vincent, M.M., Vellanti, J.A.: Specific inhibitory factors of cellular immunity in children with subacute sclerosing panencephalitis. J. Pediat. (In Press).

Steele, R.W., Fucillo, D.A., Hensen, S.A., Vincent, M.M., Bellanti, J.A.: SSPE and cellular immunity. Arch. Neurol. (In Press).

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Value of IgM Determinations in the Diagnosis of Acute Neonatal Infections.

WORK UNIT NO.: C-21-74

PRINCIPAL INVESTIGATOR: Amil Ortiz, M.D., Captain, MC

ASSOCIATE INVESTIGATORS: Melvin Baden, M.D., Lieutenant Colonel, MC

OBJECTIVES

To correlate elevations of neonatal serum IgM with the presence of an acute neonatal infection.

TECHNICAL APPROACH

Thirty-seven infants with suspected sepsis during the first 72 hours of life were selected and underwent complete "septic work-up". As part of the evaluation serum for IgM determination was obtained. Thirty healthy newborns were selected for controls; they too had serum IgM determinations.

Manpower: None

Funding: None

PROGRESS

Thirty-seven infants with suspected sepsis were studied for elevation of serum IgM. Six patients with proven sepsis by positive cultures demonstrated marked elevation in serum IgM compared to a control group. This correlated well with the presence of infection.

CONCLUSIONS: (1) Elevation of serum IgM levels correlate significantly with the presence of acute infection in neonates, (2) serum IgM levels alone should not be used to make a decision as to course of therapy,

C-21-74 (Continued)

(3) serum IgM levels correlated with the clinical presentation and historical events aid the physician in determining the aggressiveness of therapy while awaiting the more definitive results of cultures, and (4) any level of serum IgM above 20 mg% and certainly above 25 mg% in the neonate is indicative of an acute infectious process.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Preparation and Purification of Dialyzable Transfer Factor for the Treatment of Selected Infectious Diseases.

WORK UNIT NO.: C-42-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D., Major, MC
Luis Canales, M.D., Colonel, MC

OBJECTIVES

To evaluate the efficacy of transfer factor therapy for disseminated fungal or viral disease or for tuberuclosis unresponsive to the usual forms of therapy.

TECHNICAL APPROACH

Dialyzable transfer factor is prepared by the method of Lawrence from heparinized whole blood from human volunteers sensitive to the infectious agent under consideration. One unit equivalent to 10^9 lymphocytes is administered by subcutaneous injection to the patient and his clinical course evaluated. Potency of transfer factor is tested by passive transfer interdermally to a previously skin tested negative individual with subsequent challenge to the antigens at the site of injection.

Manpower: None

Funding: $1,092.41 Consumable Supplies FY 1974
$1,331.00 Consumable Supplies FY 1975

PROGRESS

One patient with disseminated coccidioidomycosis has undergone two courses of transfer factor therapy with good response noted. *In vitro* and *in vivo* cellular immunity to coccidioides have become positive following therapy.

An infant with cartilage hair hypoplasia and severe combined immune deficiency has been reconstituted with fetal thymus plus transfer factor.

C-42-74 (Continued)

The above named investigators are now working in collaboration with others in the southwest region of the United States in a protocol designed to evaluate transfer factor therapy for disseminated coccidioidomycosis.

Status: Ongoing

Steele, R.W., Sieger, B.E., Canales, L.: Transfer factor therapy for coccidioidomycosis CITSM. 69:13, 1975.

Steele, R.W., Sieger, B.E., Moore, W.L.: Therapy for disseminated coccioidomycosis with transfer factor from a related donor. Submitted for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Immunologic Parameters in Three Nonhuman Primates.

WORK UNIT NO.: C-19-75

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., Major, MC

ASSOCIATE INVESTIGATORS: William T. Kniker, M.D.
Seymore S. Kalter, Ph.D.

OBJECTIVES

To undertake a detailed analysis of host-herpes virus interaction in nonhuman primates in an effort to find factors in each of three species of nonhuman primates which are most critical to defense against infectious and oncogenic agents.

TECHNICAL APPROACH

In vivo and in vitro assays of immune function of three nonhuman primates--the baboon, the marmoset and the cebus--will be determined and correlations drawn for the known susceptibility of the latter species to infection and malignancy. After defining the status of the immune function of these animals, an effort will be made to reconstitute the susceptible species in such a way as to alter their previous predisposition to infection and malignancy specifically induced by herpes group viruses.

Manpower: None

Funding: $2,750.11 Consumable Supplies FY 1975

PROGRESS

T and B lymphocytes have been quantitated in the three animal species and the influence of thymosin in vitro has also been examined. Also relevant to the thymic dependent system both in vivo and in vitro cell mediated immune responses of the three nonhuman primate species to defined and specific viral, bacterial, fungal and chemical antigens has been completed and accepted for publication. Currently in progress are studies designed to evaluate immunotherapy in an effort to treat marmosets following induction of leukemia with herpes saimiri virus.

C-19-75 (Continued)

Thymus transplant alone was unsuccessful but preliminary studies have indicated that an anti-viral chemotherapeutic agent, adenine arabinoside, in combination with thymus transplant and transfer factor will successfully eradicate the malignant process.

Status: Ongoing

Steele, R.W., et al.: E and EAC rosettes in man and nonhuman primates and the effect of thymosin in vitro. J. Immunol. (In Press).

Kniker, W.T., Macias, E.G., Steele, R.W., Heberling, R.L., Eller, J.J.: Relative cellular immunity in 3 nonhuman primate species. Federation Proceedings 34:824, 1975.

Eichberg, J.W., Steele, R.W., Kalter, S.S., McCullough, B., Kniker, W.T.: T and B lymphocytes in nonhuman primates and effect of thymosin in vitro. Federation Proceedings 34:625, 1975.

Macias, E.G., Steele, R.W., McCullough, B., et al.: A comparison of cell mediated immunity to fungal, bacterial, viral and chemical antigens in three nonhuman primates. Submitted for publication.

"Relative Cellular Immunity in 3 Nonhuman Primate Species" presented at the Federation of the American Society for Experimental Biology, Atlantic City, New Jersey, 14-15 April 1975.

"T and B Lymphocytes in Nonhuman Primates and Effect of Thymosin in vitro" presented at the Federation of the American Society for Experimental Biology, Atlantic City, New Jersey, 14-5 April 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects on Attendees of a Course in Human Sexuality.

WORK UNIT NO.: C-34-74

PRINCIPAL INVESTIGATOR: Harry A. Croft, M.D., Major, MC

ASSOCIATE INVESTIGATIONS: Gilbert R. Kaats, Ph.D., Lieutenant Colonel, USAF
Edwin Cornelius, Captain, MSC
Tom Dolan, Sp5

OBJECTIVES

To study the existence of and extent of change in attendees of a course in human sexuality in regards to sexual attitudes, beliefs, values and behavior.

TECHNICAL APPROACH

The Human Sexuality Course has been presented at Fort Sam Houston on five occasions and at Fort Dix, New Jersey on one occasion. A total of approximately 1,000 attendees have been through the courses. Use was made of questionnaires returned from the first several hundred attendees to modify the final research instrument.

A pretest survey was administered on the first evening of the course followed by a post-test two months after the course.to evaluate the effectiveness of our objectives.

Manpower: None

Funding: None

PROGRESS

Contact has been made with LT Altobelli, Clinical Investigation Service, to program the computer for meaningful evaluation of the results of the data accumulated. From comments made by those who have attended the course, it appears that at least in some cases very dramatic changes have taken place in attitudes and behaviors.

C-34-74 (Continued)

The course has been well accepted both here at Fort Sam Houston and at Fort Dix, New Jersey, as well as by the civilian and military communities at large. It has received much publicity in military as well as lay publications. Newspaper articles have appeared in the following: Health Service Comman Mercury, Army Times, San Antonio Express, San Antonio Light, New York Times, and approximately 40 other newspapers around the country. The Associated Press Wire Services has also publicized the course.

Status: Ongoing

Croft, H.A.: A human sexuality course in the military. Military Medicine (In Press).

Croft, H.A.: Sexual information exam. Southern Medical Journal (In Press).

Interview by CBS Radio for future broadcast.

Workshop on Sex Counseling. Oblate College, San Antonio, Texas, 21 and 28 February 1975.

"A Human Sexuality Course in the Military - One Year Later." Presented at the annual meeting of National Sex Educators and Counsellors, Galveston, Texas, 7-9 March 1975.

"Research in Sex Education." Presented to graduate psychology class, Trinity University, San Antonio, Texas, 11 March 1975.

"Sex Education." Presented to students at Roosevelt High School, San Antonio,Texas, 17 March 1975.

Participated in workshop for teachers on "Adolescent Sexuality" sponsored by Planned Parenthood of San Antonio held at the University of Texas Health Science Center, San Antonio, Texas 21 and 22 March 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Gallium-67 as a Scanning Agent for Malignant Neoplasms.

WORK UNIT NO.: C-141-72

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the value of Gallium-67 Citrate as a tumor localizing agent in a variety of malignant neoplasma.

TECHNICAL APPROACH

Patients referred from the Oncology Service are considered for this investigational study. Following intravenous administration of Gallium-67 Citrate, whole body scans using a dual probe scanner or a whole body scintiscan table study are performed at 24 and/or 48 and/or 72 hours. In some cases cleansing enemas are required to provide adequate clearance of radioactivity in the stool. Abnormal localization of the radiopharmaceutical is noted from the results of whole body distribution images.

Manpower: None

Funding: None

PROGRESS

Ninety-four patients have been studied. These studies have been of significant clinical value in individual cases. However, the entire series will not be analyzed until 100 patient studies have been completed.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of Cisternography Utilizing ^{111}Indium DTPA.

WORK UNIT NO.: C-35-74

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the safety and efficacy of ^{111}Indium DTPA for cisternography studies.

TECHNICAL APPROACH

Patients referred from either Neurology Service or Neurosurgical Service are evaluated for entrance into this clinical infestigation. ^{111}Indium DTPA is administered into the lumbar subarachnoid space by standard lumbar puncture technique. Sequential images of the cerebral spinal fluid tracer are obtained at 2, 6, 24, and if indicated 48 and 72 hours using the scintillation camera. In general, early images are obtained using the scintiscan whole body table to evaluate for abnormal injection patterns. This radiopharmaceutical is imaged utilizing the dual isotope capability of the scintillation camera which increases the useful information for any given dose. When indicated, nasal pledgets are positioned and subsequently counted for radioactivity. This is useful when evaluating patients for CSF rhinorrhea.

Manpower: None

Funding: None

PROGRESS

Fifteen patients have been studied. The radiopharmaceutical has provided adequate images of diagnostic clinical quality in all cases. There have been no adverse side effects in any patient. Differences between ^{111}Indium DTPA kinetics and those of I-131 RISA have been noted.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of ^{111}Indium Bleomycin (MPI Tumor Scintigraphin™).

WORK UNIT NO.: C-3-75

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Members of Oncology Service Staff

OBJECTIVES

To evaluate the clinical usefulness of ^{111}Indium Bleomycin as a tumor specific radiopharmaceutical.

To demonstrate the types of neoplasms for which scintigraphy with ^{111}Indium Bleomycin has a high positive correlation with extent of disease.

TECHNICAL APPROACH

Patients are referred from the Oncology Service because of known or suspected neoplasms. ^{111}Indium Bleomycin is administered intravenously with whole body distribution of the radiopharmaceutical to be measured using the whole body scintiscan table and dual isotope technique. Images will be obtained at variable periods of time during the three days following administration of the radiopharmaceutical.

Manpower: None

Funding: None

PROGRESS

No patients have been entered into this protocol to date.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of the Thyroid by *in vivo* Radionuclidic Studies Utilizing I-123.

WORK UNIT NO.: C-4-75

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Carlos E. Menendez, M.D., Major, MC

OBJECTIVES

To substitute I-123 for I-131 in the routine clinical evaluation of the thyroid gland. Utilizing its superior physical properties and its increased available photon yield relative to patient dose, we hope to produce anatomic and physiologic data of higher overall quality and lower overall patient dose.

TECHNICAL APPROACH

I-123 will be substituted for I-131 for clinical thyroid procedures which require uptake studies or imaging studies of the thyroid gland function. The major advantage of this radiopharmaceutical is the significant decrease in dose to the patients. Additional benefits are the improved imaging characteristics of I-123.

Manpower: None

Funding: None

PROGRESS

No patients have been entered into this protocol to date.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: NEN Gallium-67 Citrate for Intravenous Administration.

WORK UNIT NO.: C-35-75

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Robert L. McAuley, Jr., Captain, MSC

OBJECTIVES

To evaluate clinically the NEN brand of Gallium-67 citrate.

TECHNICAL APPROACH

All persons with suspected bronchial carcinoma, thyroid carcinoma, gastric carcinoma, malignant melanoma, infectious processes and inflammation, and metastases of unknown primary tumors, as well as Hodgkin's disease, will be selected. Patients referred to the Nuclear Medicine Service with these diagnoses will be considered for entry into the study.

Gallium-67 citrate will be administered from 2-5 millicuries per subject. The product will be administered intravenously. The study will be carried out in accordance with the New England Nuclear Protocol "NYA-2 -- NEN Gallium-67 Citrate".

Manpower: None

Funding: None

PROGRESS

This is a new project.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Diastolic Augmentation Using an Intra-Aortic Balloon Pump.

WORK UNIT NO.: C-6-72

PRINCIPAL INVESTIGATOR: Robert L. Treasure, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Olyn M. Walker, M.D., Lieutenant Colonel, MC
George L. Zumbro, M.D., Lieutenant Colonel, MC
George M. McGranahan, M.D., Colonel, MC

OBJECTIVES

Patients unable to be weaned from cardiopulmonary bypass are being supported with the intra-aortic balloon. Careful physiologic monitoring in these critically ill patients is being maintained.

TECHNICAL APPROACH

The intra-aortic balloon is used in weening patients from cardiopulmonary bypass who are unable to generate satisfactory cardiac output. An intra-aortic balloon will be inserted in the descending aorta through a femoral arteriotomy and cardiac output increased by diastolic inflation of the aortic balloon by the AVCO pump timed by ECG. The effectiveness of this treatment will be determined by cardiac output, arterial and venous blood gases and pH; and urinary output. Blood trauma due to the balloon will be evaluated by serum hemoglobin.

Manpower: None

Funding: None

PROGRESS

Enough data has not been accumulated for analysis to date.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ethicon PolyTef Paste for Injection in Repair of Velopharyngeal Defects.

WORK UNIT NO.: C-20-72

PRINCIPAL INVESTIGATOR: S. R. LeMay, Jr., M.D., Colonel, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Some patients with velopharyngeal defects can be corrected by adding bulk to the posterior pharyngeal wall to make closure of the velum possible in normal speaking. Further experience utilizing investigational drug injection to add bulk necessary to improve the speech is sought.

TECHNICAL APPROACH

The investigational drug, Mentor PolyTef Paste for injection, will be used by the investigator in accordance with the following criteria: Age: over 6 years. No sex selection. Generally good health. Complete physical examination. Accurate evaluation to include cineradiography of the velum and recordings pre- and postoperative. Evaluation of competent speech therapists. The PTEE will be injected into the posterior pharyngeal wall and/or palate to provide the bulk necessary to improve velopharyngeal closure. Complete records will be kept. Reports to Mentor will be made. As many available patients as fit the criteria will be injected.

Manpower: None

Funding: None

PROGRESS

No new patients have been seen in the past two years; therefore, the study is terminated.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Enflurane (Ethrane) on Cardiovascular Function.

WORK UNIT NO.: C-12-74

PRINCIPAL INVESTIGATOR: John R. Ritzman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, Jr., M.D., Major, MC
Joel M. Kaplan, M.D.

OBJECTIVES

To assess the effects of enflurane, enflurane with N_2O, and enflurane with muscle relaxant upon the function of the cardiovascular system using a non-invasive technique.

TECHNICAL APPROACH

Two groups of six healthy young volunteers were studied prior to minor elective surgery. No premedication was given. After control measurements were recorded, the patients were anesthetized with 50% N_2O and either 1% halothane or 2% enflurane. Cardiovascular measurements were made at the end of 30 minutes of stable anesthesia; then the N_2O was discontinued and repeat measurements were made 20 minutes later. End-tidal halothane or enflurane, arterial blood gases, blood pressure, and heart rate were recorded at each measurement period.

A simultaneous recording at 100 mm/sec was made of a carotid arterial pulse trace, phonocardiogram and electrocardiogram. The intervals measured were the QS_2 (total electromechanical systole), LVET (left ventricular ejection time) and PEP (Pre-ejection period) which were all corrected for heart rate. From these intervals, PEP/LVET, $1/PEP^2$ and the ejection were calculated.

Manpower: None

Funding:			
	$1,297.70	Consumable Supplies	FY 1974
	$ 372.00	TDY	FY 1975

C-12-74 (Continued)

PROGRESS

Both anesthetic agents caused a significant increase in the PEP/LVET ratio, and a decrease in $1/PEP^2$ and the ejection fraction, indicating myocardial depression at equipotent light levels of anesthesia ($P < .05$). The difference between halothane and enflurane was significant ($P < .05$) with halothane being more depressant. Discontinuation of N_2O led to a further depression of these parameters. Arterial blood gases showed no significant differences.

Status: Completed

Presented at the annual meeting of the American Society of Anesthesiologists, Washington, D.C., October 1974.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cardiovascular Effects of Continuous Spinal, Epidural, and Nitrous-Oxide-Narcotic Anesthesia on Patients Undergoing Surgery for Hip Fractures.

WORK UNIT NO.: C-13-74

PRINCIPAL INVESTIGATOR: Robert W. J. Baird, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, Jr., M.D., Major, MC

OBJECTIVES

To determine the effects of spinal, epidrual, and general nitrous-oxide-narcotic anesthesia on cardiovascular parameters including: cardiac output, total peripheral resistance, mean arterial pressure, CVP and EKG in patients undergoing surgery for repair of hip fractures.

TECHNICAL APPROACH

Central venous pressure, arterial line and EKG monitors were placed in the patients. Measurements of cardiac output and other parameters were made in the supine and lateral position. The patients were then anesthetized with general or conduction anesthesia and these measurements repeated sevearl times during surgery.

Manpower: None

Funding:			
	$3,665.00	MEDCASE	FY 1974
	$ 428.00	Consumable Supplies	FY 1974
	$ 349.00	Consumable Supplies	FY 1975

PROGRESS

The project has been terminated because of: (1) insufficient patient number, (2) difficulty in obtaining these measurements in often demented patients, and (3) inability to provide safe anesthesia and meaningful data with the personnel presently available.

Status: Terminated

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Postoperative Analgesia for Thoracotomy Patients.

WORK UNIT NO.: C-28-74

PRINCIPAL INVESTIGATOR: Edward D. Miller, Jr., M.D., Major, MC

ASSOCIATE INVESTIGATORS: Joel A. Kaplan, M.D.
Edgar G. Gallagher, Jr., M.D., Lieutenant Colonel, MC

OBJECTIVES

To assess the effect of intercostal block using bupivacaine and dextran in patients who have undergone thoracotomy.

TECHNICAL APPROACH

Eighteen patients undergoing routine thoracotomies were studied. All patients had control chest x-rays, arterial blood gases, and pulmonary function studies preoperatively. A standard anesthetic consisting of thiopental, succinylcholine, nitrous oxide, enflurane and pancuronium was used in all patients.

Prior to closure of the incision, six intercostal spaces were injected by the surgeon with 3 ml of a randomly determined drug mixture. Patients received either: (1) bupivacaine and saline, (2) bupivacaine and dextran, or (3) saline and dextran. Arterial blood gases, pulmonary functions, chest x-rays, narcotic dosages, sensory level and subjective responses were evaluated for three days postoperatively.

Manpower: None

Funding: $173.02 Consumable Supplies FY 1974

PROGRESS

Our results in the eighteen patients studied demonstrate that intercostal nerve blocks can markedly reduce postoperative pain and improve

C-28-74 (Continued)

the pulmonary function. The most significant differences from the control patients were seen in the values of arterial oxygenation, vital capacity, and forced expiratory flow rates. The duration of the block with bupivacaine and saline was less than 12 hours, while the mean duration of the block with bupivacaine and dextran was 36 hours.

Status: Completed

Presented at the International Anesthesia Research Society meeting, Hollywood, Florida, March 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effects of Prolonged Acceleration ($+G_z$) on the Respiratory Exchange Ratio in Man.

WORK UNIT NO.: C-29-74

PRINCIPAL INVESTIGATOR: David W. Crim, M.D., Major, MC

ASSOCIATE INVESTIGATORS: F. Wesley Baumgardner, Ph.D.
Sidney D. Leverett, Jr., Ph.D.

OBJECTIVES

To determine the effects of prolonged (5-10 min.) G_z on the respiratory exchange ratio in man.

(This study was performed at the School of Aerospace Medicine, Brooks Air Force Base, Texas. The projects was registered for record only.)

TECHNICAL APPROACH

Five subjects who were experienced in riding the centrifuge using the Anti-G suit and performing the M-1 maneuver were selected and placed in the gondola of the USAFSAM centrifuge. Readings were taken at 1, 2, 3, and 4 G_z for 10 minutes and 5 G_z for 5 minutes. Readings of the 2, 3 and 4 G_z runs were compared with the average of the 1 G_z run. Continuous, breath-by-breath readings were taken on each subject from the beginning of each run until R had returned to 1 G_z levels after each run.

Manpower: None

Funding: None

PROGRESS

During prolonged acceleration ($+G_z$), there are changes in ventilation and pulmonary gas exchange. The magnitude of these changes appears to be more strongly affected by the magnitude of $+G_z$ rather than time at $+G_z$. It is felt that the increased ventilation is due in part to increased work and in part to the increased G level. No significant increase in O_2 consumption was seen in the 1, 2 and 3 G_z runs; however, there does appear to be a slight increase in consumption as the G_z

C-29-74 (Continued)

increases. This initial rise was due to the subjects preparing themselves for the run by hyperventilating and straining their muscles and not due to the initial effects of the acceleration. On the 4 G_z run, there was an immediate and significant rise in O_2 consumption in the first 30 seconds, remained high throughout the 10 minute run, and did not change significantly after the first 30 seconds. The initial rise of CO_2 output seen only at 30 seconds of the 2 and 3 G_z run was due to the subjects preparing themselves, as previously mentioned. The fact that the CO_2 remained unchanged at 1, 2 and 3 G_z, but minute ventilation increased at these levels, shows that acceleration does cause increasing dead space in the lungs. At 4 G_z the increasing ventilation was unable to keep up with the rising CO_2 and a significant change is noted. As with the O_2, it takes about 30 seconds for the CO_2 to find its new level and thereafter remains stable.

These sets of experiments clearly demonstrate that pulmonary function is significantly altered by increasing G_z forces. The increasing oxygen consumption and the inability to excrete corresponding quantities of carbon dioxide result in a falling R value. Whether metabolic changes resulting in increased lipid metabolism are in part responsible for these changes cannot be asceratined from these experiments. It would seem unlikely, thought, since these changes occur so rapidly.

Prolonged acceleration of an individual may in part be limited by his inability to excrete appropriate quantities of carbon dioxide resulting in increased blood levels of carbon dioxide. Whether such increases in carbon dioxide would result in impairment of judgment should be investigated in any project involving prolonged acceleration.

Status: Completed

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Enflurane and Halothane on Myocardial Function in the Rhesus Monkey (Macaca Mulatta).

WORK UNIT NO.: C-2-75

PRINCIPAL INVESTIGATOR: Douglas Pritchard, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, Jr., M.D., Major, MC
John R. Ritzman, M.D., Major, MC
Howard H. Erickson, Lieutenant Colonel, USAF VC

OBJECTIVES

To compare the effects of two halogenated anesthetic agents on myocardial function using an invasive technique.

TECHNICAL APPROACH

Ten Rhesus monkeys were chronically instrumented with aortic flow probes, as well as left ventricular, aortic and venous pressure monitoring devices. Ethrane or Forane anesthesia was administered and variables measured over a period of time.

Manpower: None

Funding:			
	$5,253.58	MEDCASE	FY 1975
	$ 18.00	Consumable Supplies	FY 1975
	$ 322.00	TDY	FY 1975

PROGRESS

Ten chronically instrumented rhesus monkeys were given enflurane and halothane anesthetics for a total of 18 exposures. No significant difference in max dp/dt, dp/dt/LVDP, mean arterial pressure, central venous pressure or heart rate were detected between the two agents at comparable anesthetic depths.

Additional studies have been done and data is presently being analyzed at Brooks Air Force Base.

Status: Ongoing

Presented at the Anesthesia Research Society Meeting, Hollywood, Florida, 17-20 March 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Percutaneous Cannulation of the Dorsalis Pedis Artery.

WORK UNIT NO.: C-7-75

PRINCIPAL INVESTIGATOR: John A. Youngberg, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, M.D., Major, MC
James D. Pister, M.D., Major, MC

OBJECTIVES

To evaluate the usefulness, accuracy of readings, and complication rate in cannulating the dorsalis pedis artery instead of the radial artery for monitoring patients.

TECHNICAL APPROACH

Thirty percutaneous cannulations of the dorsalis pedis artery were prospectively studied in twenty-eight patients. Patients were followed by physical examination and Doppler measurements. Arm cuff systolic and diastolic blood pressures were compared to dorsalis pedis cannulation pressures.

Manpower: None

Funding:			
	$900.00	Capital Equipment	FY 1975
	$228.00	Consumable Supplies	FY 1975

PROGRESS

It was observed that cannula systolic pressures were higher and cannula diastolic pressures were lower than arm cuff pressures. The correlation coefficients for cuff to cannula systolic and diastolic pressures were .91 and .80, respectively. Two of the thirty cannulations resulted in complete thrombosis and one additional artery showed decreased flow by Doppler measurement. In both cases of thrombosis retrograde flow distal to the occlusion was dmonstrated and in one of these cases ischemic change was noted. This ischemic change resolved over three days with no residual sequelae.

C-7-75 (Continued)

CONCLUSION: This study is felt to demonstrate that cannulation of the dorsalis pedis artery is a safe, and easily performed technique of intra-arterial monitoring.

Status: Completed

Presented at the Gulf Coast Residents Conference, Gainesville, Florida, 25 May 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Pulmonary Sequestration: A Broad Spectrum of Bronchopulmonary Foregut Abnormalities.

WORK UNIT NO.: C-15-75

PRINCIPAL INVESTIGATOR: George L. Zumbro, M.D., Lieutenant Colonel,MC

ASSOCIATE INVESTIGATORS: Robert L. Treasure, M.D., Colonel, MC
Girard Seitter, M.D., Lieutenant Colonel, MC
Tracy E. Strevey, M.D., Colonel, MC
Walter Brott, M.D., Colonel, MC
David C. Green, M.D., Colonel, MC

OBJECTIVES

The broad clinical, embryologic and radiologic spectrum of pulmonary sequestration has not been adequately emphasized. In order to gain a clearer understanding of these foregut abnormalities, all cases from the files of Brooke Army Medical Center, Fitzsimons Army Medical Center, and Walter Reed Army Medical Center will be reviewed.

TECHNICAL APPROACH

The records of the above mentioned Army medical fcilities were carefully reviewed, and thirty-three cases met the criteria for the diagnosis of bronchopulmonary sequestration. Anomalous systemic arterial blood supply to the sequestrum was documented at operation or by aortography in all patients. All mediastinal and pulmonary cystic lesions were excluded if there was no anomalous arterial supply.

Manpower: None

Funding: $493.00 IDY FY 1975

PROGRESS

Clinical manifestations varied from asymptomatic patients to those with recurrent pulmonary infection, hemoptysis and intrapleural hemorrhage. The presence of symptoms strongly correlated with air containing cystic sequestrations. Each of the 21 patients with air containing cystic sequestrations experienced recurrent pulmonary infections. Five patients had repeated hemoptysis, which was massive in one.

C-15-75 (Continued)

The embryologic spectrum was represented by 23 intralobar, six extralobar, one combination extralobar and intralobar, and two hybrid sequestrations. One patient with bilateral sequestration, proven by aortography only, probably had bilateral intralobar sequestration, since the demonstrated venous drainage was via the pulmonary veins.

Radiographic presentations in our patients included radiopaque masses; air containing cysts with and without fluid levels; and massive hemothorax. One patient presented with bilateral lower lobe masses. Upper, middle and lower lung fields were each the site of involvement; however, the region of the posterior basilar segment was most commonly involved on chest roentgenography.

All extralobar and hybrid sequestrations were excised. Five intralobar sequestrations were removed by basilar segmentectomy and the remainder required lobectomy. There were no deaths or major complications.

Status: Completed

Presented at the Society of Thoracic Surgery meeting in Montreal, Canada, January 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prevention of Ischemic Contracture of the Left Ventricle During Aortic Cross Clamping.

WORK UNIT NO.: C-21-75

PRINCIPAL INVESTIGATOR: George L. Zumbro, M.D., Lieutenant Colonel, MC

ASSOCIATE INVESTIGATORS: Olyn M. Walker, M.D., Lieutenant Colonel, MC
Loren B. Henley, M.D., Lieutenant Colonel, MC
Edward S. Rappaport, M.D., Major, MC
Robert L. Treasure, M.D., Colonel, MC

OBJECTIVES

To determine the protective effect of propanolol on the left ventricular myocardium during aortic cross clamping.

TECHNICAL APPROACH

Twenty-five mongrel dogs will be anesthetized with sodium pentobarbital and maintained on positive pressure ventilation. The heart will be exposed through a right thoracotomy and following intravenous administration of heparin the animals will be placed on cardiopulmonary bypass using routine caval and femoral artery cannulation.

Twenty animals will undergo a two hour period of cross clamping of the ascending aorta during cardiopulmonary bypass. Left ventricular venting will be done, and epicardial biopsies taken from the left ventricle prior to bypass and five minutes after removing the aortic cross clamp.

Five animals serving as controls will have no aortic cross clamping or venting of the cardiac chambers. Left ventricular epicardial biopsies will be taken prior to beginning bypass and after two hours of bypass time.

The twenty study animals will receive either 5 cc of saline or a 5 cc solution containing 20 micrograms/kg of propranolol intravenously five minutes prior to cross clamping the aorta. The study will be conducted in a double blind fashion with a disinterested person mixing the propranolol and saline solutions according to a previously arranged code.

Manpower: None

Funding: $800.00 Consumable Supplies FY 1975

C-21-75 (Continued)

PROGRESS

The laboratory aspects of this project were completed on 9 June 1975; however, the results of electron microscopic evaluation will not be completed until approximately 1 July 1975. Preliminary findings indicate that there is no difference between the propranolol treated group of animals and the non-treated group.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Biodegradable Cuffs, An Adjunct to Peripheral Nerve Repair in Dogs.

WORK UNIT NO.: C-23-75

PRINCIPAL INVESTIGATOR: Robert L. Reid, M.D., Colonel, MC

ASSOCIATE INVESTIGATORS: Stephen C. Boone, M.D., Lieutenant Colonel, MC
Donald H. See, M.D., Lieutenant Colonel, MC
Duane E. Cutright, Colonel, DC, WRAIR

OBJECTIVES

To determine the efficacy of biodegradable cuffs at the sutured site of sectioned peripheral nerves. Specifically it will be determined if the biodegradable cuff will:

a. Prevent the in-growth of fibroblasts from surrounding tissues.
b. Maintain the regenerating axonal tissue in a parallel arrangement thereby reducing neuroma-glioma formation.

TECHNICAL APPROACH

Ten adult mongrel dogs will be required for the study. The ulnar nerves in the forelimb and peroneal nerves in the hindlimbs will be surgically exposed, transected, and repaired with 9-0 nylon epineural sutures using magnification. One side will be repaired in the standard fashion and used as a control. The other side will be repaired in the same fashion, but in addition the anastomotic site will be covered with a standard copolymer cuff whose cross-section diameter is 2½ times that of the repaired nerve. The cuffs will be manufactured by Colonel Cutright at Walter Reed Army Institute of Research at no expense. No animal limb immobilization is requested following the surgery.

Nerve conduction and electromyographs will be conducted on all limbs at monthly intervals and at the time of sacrifice. The electromyographer will not know which side of the animal is the test or control. After the anastomotic site is resected, light and electronmicroscopic studies will be performed at Walter Reed Army Institute to determine the amount of local invasiveness of scar tissue and/or reaction in the nerve to the copolymer biodegradation. The results will then be correlated with the electrical studies.

Manpower: None

Funding: $1,630.18 Consumable Supplies FY 1975

C-23-75 (Continued)

PROGRESS

All materials and animals were purchased and received. The first animal surgery was conducted 27 March 1975. To date five of the ten proposed animals have had the planned surgery.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Ocular Flora of the Burned Patient.

WORK UNIT NO.: C-32-75

PRINCIPAL INVESTIGATOR: Clarence G. Prahmus, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Thomas E. Runyan, M.D., Lieutenant Colonel, MC
John C. Hoskins, M.D., Major, MC

OBJECTIVES

a. To established the incidence of individual micro-organisms in the conjunctival flora of the acutely burned patient.
b. To see if and how these flora are altered during treatment and convalescence and particularly during changes in the lid-conjunctival-corneal anatomical relationship.
c. To compare the flora recovered from the conjunctiva with those recovered from other sources (skin, IV sites, blood, surrounding enrivonment).
d. To study the incidence of ocular complications resulting either directly from the burn iteself or from secondary changes occurring during treatment and convalescence.
e. To look at the effectiveness of various prophylactic modalities of treatment (topical Lucrilube Ophth Oint; topical or local antibiotics and/or steroids; lid, conjunctival, and/or corneal surgery; bandage soft contact lenses).
f. To assess the efficacy of various therapeutic measures once these complications have occurred (bandage soft lenses with and without antibiotics, tarsorrhaphies, conjunctival flaps, keratoplasties).

TECHNICAL APPRAOCH

Each of the patients admitted to ISR is categorized into one of four groups as outlined in the protocol. A culture is obtained from each eye initially and twice a week thereafter. In indicated cases where large corneal defects are present, i.e., corneal burn, soft contact lenses are placed.

Manpower: None

Funding: None

C-32-75 (Continued)

PROGRESS

Cultures have revealed a remarkable yield of pathogens. It is too early to attach significance to the clinical picture and the recovery we have had thusfar. The soft contact lens appears to have a place in treatment of corneal epithelial defects in these patients.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: An Evaluation of Water Diuresis for the Prevention and Control of Recurrent Urinary Tract Infection in Women.

WORK UNIT NO.: C-34-75

PRINCIPAL INVESTIGATOR: Evelyn R. Anderson, R.N., Ph.D.
University of Texas School of Nursing
at San Antonio

ASSOCIATE INVESTIGATORS: Mauro P. Gangai, M.D., Colonel, MC
Carol Small Taylor, R.N., M.Sc.

OBJECTIVES

To evaluate the effect of teaching principles of fluid diuresis tc females on the prevention and control of urinary tract infection.

TECHNICAL APPROACH

Each patient in the experiment will be given a hydrometer and instructed in its use. Specific gravity readings will be taken each morning on the first urine sample. It will be recommended they increase their fluid consumption to 200-3000 ml/day depending upon such variables as fever, vomiting, diaphoresis, diarrhea, the presence of symptoms of urinary discomfort, and the specific gravity readings. Daily recordings will be kept of their specific gravity, fluid intake, and any special remarks the patient wishes to make. Both the experimental and control group will be contacted monthly to inquire about their health and to insure that no complication has developed that would contraindicate continuing in the experimental group. The number of infections over a one year period will be compared to each patient's previous record.

Manpower: None

Funding: None

PROGRESS

This is a new project.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

APPENDIX A

SOUTHWEST ONCOLOGY GROUP STUDIES

Manpower: None

Funding: $1,441.80 Contractural Service FY 1975

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DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination and Single Drug Therapy in Breast Cancer

WORK UNIT NO.: SWG 450

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To determine the relative efficacy of two combination chemotherapy regimes in patients with breast cancer.

2. To determine the efficacy of single new agents in breast cancer patients who have received no prior chemotherapy.

TECHNICAL APPROACH

Patients entering the study will receive therapy on a randomized schedule as prescribed by the study protocol. Approximately 50 patients will be studied in the combination therapy group (Vincristine, Methotrexate, 5-FU, Cytoxan and Prednisone) and 30 in the single agent group (Adriamycin).

PROGRESS

The Southwest Oncology Group reported the results of this study at the XI International Cancer Congress in Florence and they form the basis for the current study of adriamycin. The Group has a combined experience in 315 patients in four completed studies. The overall percentage of response is 40 in patients without prior chemotherapy and 30 in patients with prior chemotherapy.

Submitted to Cancer Research for publication.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adriamycin, 5-FU, Cyclophosphamide and Methotrexate for Advanced Breast Cancer.

WORK UNIT NO.: SWG 7405

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To test three different drug combinations utilizing adriamycin as the base drug in the treatment of patients with breast cancer who have received no prior chemotherapy in order to: (1) determine the relative efficacy of adding drugs singularly or in combination to adriamycin and (2) determine the comparative toxicity of the regimens.

TECHNICAL APPROACH

This study is designed to determine whether adriamycin + 5-FU + cyclophosphamide + methotrexate or adriamycin + 5-FU + cyclophosphamide results in a significantly higher response rate than adriamycin + 5-FU. Approximately 76 patients will be entered into each treatment group. Each of the above regimens will be administered according to the schedule outlined in the study protocol.

PROGRESS

Seventy patients have been entered into the study. Since only nine of the patients entered are currently evaluable, it is too early to make a thorough analysis of the study. One of the nine patients has been in complete response, three have had partial responses, and five have had no responses. The four responses have all been in patients without liver involvement.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chromomycin A_3 for Advanced Breast Carcinoma.

WORK UNIT NO.: SWG 7408

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To investigate the effectiveness of Chromomycin A_3 in the treatment of advanced breast carcinoma.

TECHNICAL APPROACH

Approximately 25 patients will be enetered into the study. Chromomycin will be administered daily x 5 days through an establishing running IV. Five consecutive days of treatment constitute a course of therapy. Two courses of treatment with toxicity will constitute an adequate trial.

PROGRESS

Twenty-one patients have entered the study most of whom are too early to evaluate. Only four patients are evaluable, two of which had no response and the other two had increasing disease.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: 5-Azacytidine in Patients with Acute Leukemia

WORK UNIT NO.: SWG 7209

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To determine the effectiveness of 5-Azacytidine in the treatment of acute leukemia.

TECHNICAL APPROACH

A minimum of 14 evaluable patients in each of the major diagnostic groups (acute lymphocytic leukemia and acute myelocytic leukemia) will be entered into the study. Remission induction and remission maintenance dosages will be administered according to the study protocol.

PROGRESS

A total of 65 patients have been registered of which 54 are evaluable. There were 24 patients with an adequate trial of whom 33% achieved complete remission and an additional 5 of 24 patients had a partial remission. The longest duration of remission is in a 36 year old woman with a duration of greater than 534 days. Toxicity continues to be a problem and is manifested by nausea and vomiting and prolonged myelosuppression.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Study of Adriamycin in Adult Acute Leukemia.

WORK UNIT NO.: SWG 448

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To determine the efficacy of adriamycin in the remission induction of adult acute leukemia and to evolve an appropriate therapeutic regimen for this study and as a point of reference for future possible drug combinations with this agent.

TECHNICAL APPROACH

All patients registered for this study will receive adriamycin by a single IV injection. Therapy will continue according to the schedule outlined in the protocol study.

PROGRESS

Complete or partial response has been noted in 23 of 70 evaluable patients. (This study was replaced by SWOG 7401.)

Status: Ongoing at Brooke Army Medical Center

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Busulfan in Chronic Granulocytic Leukemia.

WORK UNIT NO.: SWG 545/546

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To evaluate and compare intermittent and continuous remission-maintenance therapy with oral busulfan in chronic granulocytic leukemia.

TECHNICAL APPROACH

Patients with previously untreated chronic granulocytic leukemia will be allocated in random pattern and in equal numbers to one of two treatment programs for the study of remission-maintenance as prescribed in the study protocol. The initial remission-induction shall be with daily oral busulfan in the same dose for both groups as described in the study protocol.

PROGRESS

Ninety-one of 116 registered patients were evaluable. Response rates were as follows:

complete	-	65 (71%)
partial	-	16 (18%)
mixed	-	2 (2%)
none	-	1 (1%)
increasing disease	-	7 (8%)

Median length of remission: continuous - 27 months; intermittent - 37 months. (This study was closed by the Southwest Oncology Group.)

Status: Ongoing at Brooke Army Medical Center

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: POMP Combination Chemotherapy of Adult Acute Leukemia.

WORK UNIT NO.: SWG-920

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INTESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To evaluate the frequency of remission induction in adult acute leukemia.

TECHNICAL APPROACH

Adult patients with acute leukemia are treated with a combination of 5-mercaptopurine (Purinethol), Vincristine (Oncovin), Methotrexate and Prednisone (POMP) for remission induction and maintenance.

PROGRESS

This study was completed by the Southwest Oncology Group in July 1973. However, it remains open at Brooke Army Medical Center for treatment of patients entered into the protocol study.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Three Combination Regimens (OAP, DOAP, COAP) for Remission-Induction and Remission-Maintenance Therapy for Adult Leukemia.

WORK UNIT NO.: SWG 560/561

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To compare the effectiveness of three drug regimens above.
2. To estimate the effectiveness of these three regimens when cytosine arabinoside is given by 120 hour infusion.
3. To compare two maintenance regimens: intermittent remission reinduction vs. intermittent reinduction plus continuous 6MP.

TECHNICAL APPROACH

Each of the three regimens are administered every two weeks. Vincristine is administered intravenously once every two weeks. Prednisone is administered orally for five days every two weeks. Cytosine arabinoside is administered intravenously as a 120 hour continuous infusion every two weeks. Cytoxan is administered as a single rapid intravenous injection daily for five days every two weeks. Daunomycin is given as an intravenous injection once every two weeks.

PROGRESS

This study has been closed by the Southwest Oncology Group. However, it remains open at Brooke Army Medical Center for treatment of patients entered into the study protocol.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Remission-Induction for Adult Acute Lymphocytic Leukemia with Adriamycin, Vincristine and Prednisone Remission-Maintenance with Methotrexate and 6-Mercaptopurine Reinforcement with Prednisone and Vincristine.

WORK UNIT NO.: SWG 7401

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To evaluate the effectiveness of Adriamycin, Vincristine and Prednisone in the induction of remission in acute lymphocytic leukemia in adults.
2. To evaluate the following remission maintenance program: daily 6-mercaptopurine and weekly methotrexate, plus periodic reinforcement with prednisone and vincristine.

TECHNICAL APPROACH

Patients who have received no prior adriamycin and who have ALL with at least 30% blasts in the marrow are eligible for entry into the study. Only adults 15 years of age or older will be studied. Approximately 37 patients will be entered. The remission-induction and remission-maintenance phases will be administered according to instructions in the study protocol.

PROGRESS

The complete remission rate was 67% in 15 evaluable patients and 91% in patients with an adequate trial.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Remission-Induction for Adult Acute Leukemia with Ten-Day OAP; Remission-Maintenance with OAP vs. OAP plus BCG.

WORK UNIT NO.: SWG 7315/7316

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To test the remission induction efficacy of ten-day OAP in adult acute leukemia.

2. To compare the effectiveness of 5-day maintenance OAP with 5-day maintenance OAP plus BCG in prolonging the duration of complete remission of patients achieving a complete remission on 10-day OAP induction which was followed by 5-day OAP consolidation.

TECHNICAL APPROACH

A minimum of 135 patients will be entered into the remission-induction phase of the study. OAP will be administered x 10 days as prescribed by the study protocol. Bone marrow aspirations will be done on day 14 and every 4 or 5 days thereafter to determine when the marrow is cleared of leukemic cells and when recovery from the marrow hypoplasia has occurred sufficient to start the next course. Following the second induction course of OAP the bone marrow will again be allowed to recover. If the patient achieves a complete remission after the second course of OAP, he will then receive three consolidation courses of 5-day OAP therapy.

PROGRESS

SWG 7315 - This protocol was closed for further patient entries by the Southwest Oncology Group, 8 October 1974. The conclusion was that the ten-day OAP is better than any prior remission induction therapy that has been investigated by the Group. The complete response rate for ten-day OAP is better than that for five-day OAP at the .05 level. Correction for prognostic factors still gives a probability that this is better than five-day OAP by approximately 90%. This is a very important study

SWG 7315/7316 (Continued)

for the Group since it is the first non-randomized historically controlled Groupwide study and it provides a very important new technique.

SWG 7316 - This is an extremely important study since it forms the pattern for future combined immunotherapy-chemotherapy studies. At this time, it is too early to calculate survival rates in the maintenance phase of the study.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Colorectal Carcinoma Comparing Bolus Weekly 5-FU vs. the Combination of Methyl CCNU plus Bolus Weekly 5-FU.

WORK UNIT NO.: SWG 7302

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To estimate the effectiveness of the combination therapy and 5-FU alone.

To determine whether the objective remission rate of the combination therapy is significantly superior to that of 5-FU alone.

TECHNICAL APPROACH

All patients prior to recieving the drugs will be randomized between the two arms of the study. The randomization will be designed so that three patients will receive 5-FU plus MeCCNU for every patient on 5-FU. Patients will be stratified into two groups: Patients with liver metastases only; patients in all other categories combined (including those with liver metastases plus metastases to other sites). Therapy will conform to the schema outlined in the study protocol.

PROGRESS

This study was closed by the Southwest Oncology Group in October 1974. However it remains open at Brooke Army Medical Center for registered patients.

The following conclusions have been reached:

1. Weekly 5-FU had overall rate of 12% with little toxicity.
2. 5-FU+MeCCNU had overall response rate of 28% with significant toxicity.
3. Response rate with combination is not different between patients with liver metastasis alone and other sites.

SWG 7305 (Continued)

4. All 5-FU responses occurred in "other site" disease.
5. No differences existed in response between colon cancers and other GI sites.
6. Combination of 5-FU and MeCCNU is cumulatively toxic.
7. Natural history data was consistent with prior reports regarding sites of primary lesions and patterns of metastases. More men were in this study group than predicted. "Disease free interval" in patients with liver metastasis alone was quite short.

Status: Ongoing at Brooke Army Medical Center

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATIONAL PROJECT RESUME

TITLE: Chemotherapy of Disseminated Testicular Carcinoma with Vinblastine and Bleomycin or Actinomycin-D, Bleomycin and Vincristine.

WORK UNIT NO.: SWG 7303

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To compare the relative effectiveness of velban and bleomycin vs. vincristine, bleomycin, and actinomycin-D in the remission induction of disseminated testicular carcinoma.

2. Attempt at recruitment of partial responses into the complete response pool via a crossover mechanism involving the above agents (reinduction).

TECHNICAL APPROACH

All patients with stage III (supradiaphragmatic) metastatic testicular carcinoma are eligible to enter the study regardless of prior radiation or chemotherapy, except for those patients who have had a trial of one of the selected chemotherapeutic agents. Patients will be randomly assigned to receive vinblastine/bleomycin or actinomycin-D/vincristine/bleomycin. Therapy will conform to the outline given in the study protocol.

PROGRESS

The efficacy demonstrated in all Dixon-Moore classes is unlike the experience with mithramycin. Response rate is highest in embryonal cell carcinoma and the two regimens appear comparable in this category. The vinblastine/bleomycin limb appears superior for the first time.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Combined Radiotherapy and Chemotherapy for Stages II-B, III-A and III-B Hodgkin's Disease.

WORK UNIT NO.: SWG 160

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To determine the safety and effectiveness with which total nodal radiotherapy could be given following MOPP chemotherapy in patients with II-B, III-A, and III-B Hodgkin's disease.

TECHNICAL APPROACH

The major criterion for study is the toxicity in the radiation portion of this protocol. The study was initially begun with three cycles of MOPP, subsequently escalated to four cycles of MOPP and after sufficient experience had been gained it was anticipated to go to six cycles.

PROGRESS

A definitive analysis of this study was not accomplished by the Southwest Oncology Group coordinator. However, the radiotherapist from Wilford Hall USAF Medical Center reviewed his experience with the delivery of radiotherapy on this protocol in a total of 23 patients. Twelve patients had completed the study after receiving three cycles of MOPP and 11 patients completed the study after receiving 4 cycles of MOPP. Based on their data, there is no evidence that for a difference in the patient's tolerance to radiation therapy whether 3 or 4 cycles of MOPP precedes the radiotherapy. Accordingly, the Wilford Hall Group will escalate to 5 cycles of MOPP in 5 patients and, if tolerated, to 6 cycles of MOPP.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Methyl CCNU for the Treatment of Various Solid Tumors Except Carcinoma of the Breast

WORK UNIT NO.: SWG 7200

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATOR: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To evaluate the effectiveness of intermittent oral methyl CCNU in the treatment of various solid tumors.

TECHNICAL APPROACH

All patients with measurable solid tumors who are not eligible for higher priority protocols or more conventional chemotherapy are eligible for study. The exceptions for admission to the study are outlined in the protocol. Therapy will conform to the schema outlined in the study protocol.

PROGRESS

This study remains open for Hodgkin's disease only.

Status: Ongoing

Tranum, B.I., Gottlieb, J.A., Haut, A., Rivkin, S. and Weber, E.: Methyl CCNU in Hodgkin's Disease and Other Tumors. Accepted for publication, Cancer.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hodgkin's Disease: Remission Induction with MOPP + Bleomycin.

WORK UNIT NO.: SWG 774/775

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To determine the comparative effectiveness of MOPP alone and in combination with two different dose schedules of bleomycin for complete remission and induction in patients with disseminated Hodgkin's disease.

2. To determine the relative effectiveness of MOPP and radiation therapy followed by MOPP and intensive MOPP in remission consolidation in those patients achieving complete remission.

TECHNICAL APPROACH

All patients will be randomly assigned to either MOPP alone, MOPP plus low dose bleomycin, or MOPP plus high dose bleomycin. All patients will initially receive MOPP treatment in full doses if they have adequate bone marrow reserve, and half doses if they have moderately impaired bone marrow reserve. Six courses of such treatment either with or without bleomycin will be given. For patients who are in complete remission after six courses of treatment, randomization to three remission consolidation treatment groups will be achieved. Following consolidation treatment, no further treatment will be administered and the patient will be followed until relapse. Patients who achieve a partial remission will continue monthly courses of MOPP alone to complete remission. Patients who, in the judgment of the cooperating radiotherapist, cannot tolerate 4000 rads in four weeks to the area of major involvement, prior to the institution of remission induction, will be separately randomized to the first and third consolidation limbs. Approximately 75 patients will be entered into each phase of the study.

SWG 774/775 (Continued)

PROGRESS

A total of 183 patients have been finally evaluated, showing an overall complete response rate of 74%. There is a statistically significant difference (at the 5% level) in the complete response rate for patients receiving MOPP alone (67%), MOPP + low dose bleomycin (85%) and MOPP + high dose bleomycin (72%).

This study has been completed by the Southwest Oncology Group and the data were presented at the 11th International Cancer Congress in Florence Italy by Dr. Coltman.

Status: Ongoing at Brooke Army Medical Center

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Radiotherapy-Chemotherapy (MOPP) for Stages I and II A and B Hodgkins.

WORK UNIT NO.: SWG 781

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To compare total nodal radiotherapy and involved field radiotherapy plus MOPP chemotherapy in patients with Stages I and II, A and B Hodgkin's disease.

TECHNICAL APPROACH

At the time of registration of the patient, randomization to one or two treatment programs will be made: (1) total nodal radiation, or (2) involved field radiation followed by MOPP chemotherapy. Therapy will be administered according to the schedule outlined in the study protocol.

PROGRESS

Seventy-two evaluable and partially evaluable cases are included in this analysis. Fifty seven patients have completed the remission induction portion of the protocol and 55 (96%) have achieved complete remission. It should be emphasized that this analysis does not include a definitive evaluation of the radiotherapy portion of the study. To date 3/27 patients have relapsed on the total nodal limb and 1/28 on the involved field + MOPP limb. The duration of remissions for TNRT range from 0 to 104 weeks and from 0 to 100 weeks for involved field + MOPP. There is no significant difference between remission duration curves.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Cyclophosphamide, Vincristine, Prednisone and Bleomycin for Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWG 780

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To determine the side effects and toxicity of a combination of bleomycin with cyclophosphamide, vincristine, and prednisone (COP) in patients with disseminated non-Hodgkin's malignant lymphoma.

TECHNICAL APPROACH

Approximately 80 evaluable patients in each of the two major malignant lymphoma categories - lymphosarcoma and reticulum cell sarcoma - should be sufficient for the study. Dosage and treatment will be according to the schedule outlined in the study protocol.

PROGRESS

This protocol was completely revised at the Southwest Oncology Group Meeting in October 1974. A revised COP #4 was activated for patient accrual so as to accumulate more information on patient responses to the COP + Bleomycin in the lower dose. The revised protocol incorporates into it the systematic restaging concepts of the new non-Hodgkin's lymphoma protocol.

Status. Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: VP 16-213 (4^1-Dimethyl-Epipodophyllotoxin-B-D-Ethylidene Glucoside) by Intravenous Infusion on Five Consecutive Days Every Three Weeks in Adults with Hodgkin's Disease and Non-Hodgkin's Lymphomas.

WORK UNIT NO.: SWG 7407

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To determine the efficacy of VP-16 in adult patients with Hodgkin's disease and non-Hodgkin's lymphoma.

TECHNICAL APPROACH

Approximately 24 patients will be studied in each group. The initial dose of VP 16-213 will be administered by IV infusion daily for five consecutive days. Courses will be administered at three week intervals as tolerated. Subsequent courses should not be repeated until the nadir of blood counts has been reached and the counts are recovering. Subsequent doses will be administered in accordance with the schedule outlined in the study protocol.

PROGRESS

One evaluable case, a patient with stage IV nodular sclerosing Hodgkin's disease, achieved a partial response on day 14 of the first course and was still active on day 26. The patient has only a small residual lymph node remaining.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy Study of Metastatic Sarcomas.

WORK UNIT NO.: SWG 7402

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To determine the efficacy of combination chemotherapy with two four-drug regimens in patients with metastatic sarcoma. The four-drug combinations are CY-VA-DIC (cyclophosphamide, vincristine, adriamycin and DIC) and CY-VA-DACT (cyclophosphamide, vincristine, adriamycin and actinomycin D).

2. To determine the efficacy of two cross-over regimens - methyl CCNU and actinomycin D - for patients failing CY-VA-DIC and methyl CCNU and DIC for patients failing CY-VA-DACT.

3. To determine the survival pattern of patients on this study compared with previous adriamycin-containing combinations in patients with metastatic sarcoma.

TECHNICAL APPROACH

Approximately 75 patients on each of the four-drug induction limbs will be evaluated. Dosage and treatment will be in accordance with the schedule outlined in the study protocol.

PROGRESS

With 98 patients evaluated, CY-VA-DIC appears to be slightly superior to CY-VA-DACT, but the response rate of both is in excess of 50%. Chondrosarcoma is beginning to show evidence of being responsive. Toxicity has been predominantly moderate to severe leukopenia and nausea and vomiting, but generally acceptable. Accrual has begun on the crossover arms of MeCCNU + actinomycin D versus MeCCNU + DIC, but it is too early to reach conclusions.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Two Combination Chemotherapy Programs in the Treatment of Disseminated Malignant Melanoma.

WORK UNIT NO.: SWG 7216

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To compare two slightly different combination programs - DIC, BCNU and Hydrea versus DIC, VCR, BCNU and Hydrea - on the frequency, magnitude, duration of tumor regression and survival in patients with disseminated malignant melanoma.

TECHNICAL APPROACH

Approximately 75 patients will be entered into the study. Dosage and treatment will be as outlined in the study protocol.

PROGRESS

The response rate for all patients on BHD is 26% and on BHD-V, 25%. For evaluable patients, the response rate is 32% and 31%. This is unchanged from the last four analyses. This study is closed pending activation of the new chemoimmunotherapy protocol by the Southwest Oncology Group.

Status: Ongoing at Brooke Army Medical Center

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Maintenance Chemotherapy of Responsive Patients with Multiple Myeloma.

WORK UNIT NO.: SWG 7313

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

To compare a combination of mephalan-cytoxan-BCNU-predrisone (MCBP) with azathioprine-prednisone plus MCBP reinduction in the long term remission maintenance of responsive patients with multiple myeloma.

TECHNICAL APPROACH

Eligible responsive patients will be registered and maintenance randomization will be by each induction regimen (MAP, MCP, MCBP). Treatment will be as outlined in the study protocol. Approximately 30 patients will be randomized into each of the remission maintenance groups.

PROGRESS

Patients with more than a 75% reduction in tumor mass are assigned to treatment with either azathioprine-prednisone (with periodic MCBP reinforcement) or indefinite MCBP. Forty-five eligible patients have been registered and all but four patients remain in good remission. Further analyses are necessary before any meaningul conclusions are reached.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy for Patients with Multiple Myeloma.

WORK UNIT NO.: SWG 734/736

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To evaluate the frequency of remission induced by a four drug induction regimen (Melphalan, prednisone, procarbazine, vincristine).

2. To compare best known maintenance with no maintenance treatment.

TECHNICAL APPROACH

Patients at Brooke Army Medical Center continue treatment according to the schedule outlined in the study protocol.

PROGRESS

This study has been closed by the Southwest Oncology Group. However, patients registered under this protocol continue therapy but are not evaluable at this time.

Status: Ongoing at Brooke Army Medical Center

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy of Multiple Myeloma in Previously Untreated Patients.

WORK UNIT NO.: SWG 7305/7306

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To evaluate the frequency and degree of response from treatment with a melphalan-adriamycin-prednisone combination (MAP), a melphalan-cyclophosphamide-prednisone combination (MCP), and a melphalan-cyclophosphamide-BCNU-prednisone combination (MCBP) in patients with previously treated multiple myeloma.

2. To compare the results with recent historical controls of patients treated with other melphalan-prednisone combinations.

TECHNICAL APPROACH

Dosage and treatment schedule will conform to the schema outlined in the study protocol. Approximately 100 patients will be entered into the study.

PROGRESS

7305 For six month treatment trials, the response rate of about 40% for each treatment is almost identical to that resulting from previous SWG studies with other melphalan-prednisone combinations. The response rate with MCP is the highest, but there are no statistically significant differences.

7306 This protocol evaluates crossover treatments for patients with less than a 75% tumor reduction. So far, only a few patients have

SWG 7305/7306 (Continued)

responded and the frequency (about 15%) is similar to the incidence that one would expect from slow onsets of remission after six months. Only rare patients have shown a marked change in the slope of the curve for tumor mass plot with the crossover treatment.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: CHOP vs HOP Combination Chemotherapy for Remission Induction and COP vs OAP Combination Chemotherapy for Maintenance in non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWG 7204/7205

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

1. To compare the remission inducing effectiveness of the 4-drug regimen -- Cytoxan, hydroxyldaunomycin (adriamycin), oncovin, and prednisone...CHOP -- to the 3-drug regimen -- hydroxyldaunomycin, oncovin, prednisone ... HOP -- given by similar schedules.

2. To compare two maintenance arms after complete remission induction and remission consolidation. One arm will utilize cyclophosphamide, vincristine and prednisone (COP) and the other arm, cytosine arabinoside, vincristine and prednisone (OAP).

TECHNICAL APPROACH

Approximately 100 valid patients on each major induction limb should permit successful evaluation of this protocol. Courses of therapy will be instituted at two week intervals. Dosage modifications will be made for subsequent courses depending on the patient's response. Dosage and treatment intervals will be in accordance with the schedule outlined in the study protocol.

PROGRESS

There is not a statistically significant difference in complete response rates in patients receiving CHOP (55%) or HOP (50%). Evaluation of the maintenance limb indicates that the OAP limb remains better than the COP limb, but the difference is not yet statistically significant.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Immunotherapy and Chemotherapy in Localized Osteogenic Sarcoma.

WORK UNIT NO.: SWG 7317

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., Major, MC

ASSOCIATE INVESTIGATORS: Hayden G. Braine, M.D., Major, MC

OBJECTIVES

Evaluation of the efficacy of the combination of transfer factor and combination chemotherapy (COMPADRI II-Cyclophosphamide, Oncovin, Methotrexate, Melphalan and Adriamycin SWOG 7317 study) in localized osteogenic sarcoma.

TECHNICAL APPROACH

Transfer factor will be administered in dosage levels of two units per day for a total of eight units to be given prior to the initiation of chemotherapy completing the administration 48 hours prior to treatment. Thereafter, during the 250 day outlined chemotherapy treatment plan, the transfer factor will be given during lapses in chemotherapy, 14 days from day one of the pulses of therapy and in the amount of 2 units per day for 2 days or 4 units total. The patients will receive approximately 40 units by the end of the prescribed 350 day course.

Chemotherapy will be administered according to the protocol plan in SWG Study 7317.

PROGRESS

This is a new study, and there are no evaluable patients at this time.

Status: Ongoing

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